MAR 25 1935

Vol. 6 MARCH, 1935 No. 3

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THE JOURNAL OF PEDIATRICS

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A MONTHLY JOURNAL DEVOTED TO THE PROBLEMS AND DISEASES OF INFANCY AND CHILDHOOD

Official Organ for
THE AMERICAN ACADEMY OF PEDIATRICS

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Published by THE C. V. MOSBY COMPANY, 3523-25 Pine Blvd., Saint Louis, U. S. A.

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The Journal of Pediatrics

VOL. 6 MARCH, 1935 NO. 3

Original Communications

GOOD PRACTICE IN MODERN EDUCATION

THE PEDIATRICIAN AND THE PEDAGOGUE

PERRY DUNLAP SMITH
WINNETKA, ILL.

THERE are so many problems which the modern pediatrician and the modern pedagogue share in common that I welcome most earnestly this opportunity to discuss with you some of them in the hope that we may come to a more complete understanding, not only of each other's practice but particularly of each other's aims and ideals.

In listening to the discussions at the meeting of the Academy this morning and this afternoon, I was very much struck by the similarity in points of view which the more modern physician and the more modern teacher hold in common. Both the teacher and the doctor are doing their best to search out the fundamental *causes* of the child's disorders and treat them rather than the *symptoms*, which for so many years apparently have been the center of attention in both professions. In this respect the doctors at present are far ahead of the teachers, but in all good modern schools you will find earnest attempts to recognize the difference between a symptom and a cause of disorder and to regard most unsocial or unusual behavior and even slowness of learning as a symptom of something rather than an evil in itself.

I am very much struck by the frequent reiteration, not only in the discussion this afternoon but also in several of the pamphlets written by members of your Academy, of the statement that in treating the child's physical disorders it was necessary always to bear in mind that he was a unit and that such an integrated whole could not be handled piecemeal. This, too, is good practice in modern education, but not always remembered by those who profess it. Just as in medicine, in education it is not possible to handle the child in pieces; to try to build his character at one time, his physical attributes at another, and to pay attention to

Address before Region III of the American Academy of Pediatrics, Rochester, Minnesota, Oct. 4, 1934.

his mental qualities at a third time. He is learning and growing all of the time and in almost every direction; in fact, just as in medicine, that child who grows in a most well-rounded manner in all directions seems to be the most satisfactory personality in the end.

A third point which we share in common is the fact that the primary and secondary school teachers at least are dealing with the growing organism, just as the pediatricians are, in contrast to many other of the specialists. When you are dealing with a growing organism, you have a very different problem from that which you face in dealing with one which has reached maturity. We make the mistake in schools (just as many general practitioners used to) of forgetting that a growing organism is not necessarily merely a smaller or less mature specimen of the finished product. It has an entity and personality all its own, and it behaves in a characteristic fashion in each of the several phases through which it passes; one of the most unfortunate fallacies which can be held by those who come in contact with the individual is that adult rules and patterns of behavior should be expected from or imposed upon individuals in the growing stage. Each child has his own type of behavior and checks and balances, which if allowed to grow normally usually will take care of his needs. However, the teacher must understand them just as the physician must understand them in his work.

This brings me to a fourth point which we share in common; that is the importance of the home, the family, and particularly the mother in the life of the growing child. I have heard frequently during this meeting the familiar phrase which one hears all too often among schoolteachers when they are trying to diagnose and prescribe for a given case, namely "the real difficulty with this case is not so much the child himself as his mother" or "I know exactly what would cure him, but you could not get the mother to carry through such a program." This problem I believe is one in which we can prove to be of great use to each other. It frequently has been my good fortune to have an intelligent pediatrician interpret to the mother the attitude of the school regarding a certain child's behavior and the remedy suggested by the school therefor; it also has been my good fortune several times to have been able to help the parent understand the attitude and methods of the pediatrician in whose hands her child had been placed. I feel that without a doubt at least 50 per cent of the problems of a good school is the education of the parents of its children, and I suspect very strongly that this holds equally true in the case of the pediatrician.

If then we share these tasks in common and if (as I firmly believe) the school's difficulties are greatly lessened by the presence of one or two good pediatricians in the community, so too I feel sure that the work of the pediatrician is greatly benefited by the presence of a good school among his clientèle. Therefore, is it not plausible for the pediatrician to bring about the presence of such schools in his community? It has

been my experience that a good pediatrician is a man of tremendous influence among the families of his patients, and if he has a firm grasp of the possibilities which education possesses for helping the growth of the children in his community, he can bear no small amount of weight in determining the type of schools which the community will demand. Therefore, it is my purpose this evening to try to place before you a few criteria which I consider important in judging the worth of a good school. If the pediatrician can indoctrinate his community with such standards of judgment regarding matters of education, I feel confident that he will be doing a great service to the country.

In setting up such criteria, I am at once struck by the fact that again we have many things in common, for in general it is very safe to say that what is a good principle in pediatrics is also a good principle in education. For example, I have just read again Dr. C. Anderson Aldrich's pamphlet, "The Feeding of Children." This pamphlet is a perfect exposition of good practice in a modern school. At the outset of the article Dr. Aldrich admits that "no force in the world can make a child eat who doesn't want to do so." Substitute the word "learn" for "eat" and you have a highly important underlying principle of modern education, however, one seldom admitted by teachers and even less seldom by parents. Dr. Aldrich then goes on to explain the error so firmly held by so many who attempt this impossible task by stating that the crux of the matter is that what you are trying to do is not so much to get a certain amount of food into the child, but to develop an attitude in him whereby he will eat normally and naturally of his own free will. By forcing the child and coercing him by violent means you may so establish an obstinate attitude that he will become a feeding problem for the rest of his life. Dr. Brennemann once told me that when he started to practice pediatrics not 10 per cent of his cases were feeding problems but that today the figure is much closer to 80 per cent. He accounts for this by the fact that parents have come to know a little bit about calories and vitamins and that standard weight charts are much more common in the homes than they used to be. As you know, calories are easily measured and since the publication of Dr. Holt's excellent book for the benefit of mothers, mothers have taken from his work those parts which they can understand more readily and check up on easily and now make a tremendous effort to get the required number of calories into the child. When the child is left to himself—as Dr. Clara Davis' work at the Children's Memorial Hospital in Chicago proved—he experiments with various foods freely but finally arrives at a balance which proves to be about the best possible for him. There are occasional meat or starch jags, but these are followed by a brief fast and then a return to the normal diet. This is an exact parallel of what has happened in education. Parents have taken information and facts (as measured by percentages in the school, which certainly are far less

scientific and accurate as methods of measurement than the usual method employed for calories) to be the most important part of a child's education and then have endeavored to see to it that their children consumed or had stuffed into them a certain number of facts per day. These being most easily measured and the percentages, or grades, being most easily understood at home, it is not strange that great overemphasis should be placed upon them, with the same results with which you are familiar in pediatrics.

Therefore, one test of the worth of a modern school is to see whether it places the major part of the emphasis on attitudes—particularly attitudes toward learning and life. If we could persuade the parent to leave the child alone, simply seeing that the environment offered ample opportunities for normal growth, nine times out of ten the child would be cured just as he is in the feeding problems.

Moreover, the better modern schools are concerning themselves with fundamental relationships between facts rather than with the facts themselves. The facts are a means to an end and not an end in themselves. The attitude of the child toward his work, the methods he uses to do something, seem to the modern teacher to be far more important than the subject matter in which he is studying. But here, of course, we have to contend with the parents. It is so easy for them to overemphasize the importance of information to their children that they do not feel that a child is growing unless he has acquired a new set of facts to add to his store of "learned lumber" each day—never realizing that although the lumber be piled in exceedingly neat piles in the child's head, for the most part it never will be used to build anything.

In this connection it is interesting to note that some of the better psychiatrists today seem to find plenty of evidence to substantiate a belief that the same perverse attitudes which are set up in a child by a forceful feeding regime imposed upon him by his parents at an early age persist into his later high school behavior. I had an interesting experience just the other day in consulting a well-known Chicago psychiatrist regarding one of my high school girls, who at the age of sixteen seemed totally incapable of accepting information either from teachers or books in spite of an extraordinarily high intelligence quotient. When I laid her symptoms before the doctor and gave him the history of the case as far as I had it, he said to me at once, "That child was a feeding problem when she was an infant."

"How can you tell that?" I said.

"They always are," he replied.

I checked up the matter and found a history of one of the most obstinate feeding difficulties that I ever have encountered. Since that time I have found six or seven other cases of persistent resistance to adult instructions or help which also developed from an attitude created in infancy by forcing the child to accept food without setting up a satisfactory attitude toward feeding.

In my school I have found that the same type of treatment which was laid down by the pediatricians for helping cure difficult feeding cases is of benefit to the high school behavior problem of this type. If we can get the attitude of the parents changed from one of a feeling of personal affront because the child won't do as he is told to one of cooperative interest in trying to solve a difficult problem, I believe that both the teacher and the doctor will be assisted greatly.

Another aspect of the problem, and one which strikes me as a highly important matter when one is attempting to judge the worth of a school, is that of the application of the fundamental laws of learning to the curriculum and to the child's behavior. We have learned a great deal in the last twenty-five years about the science of education and of child psychology; much which we have learned has become confused in people's minds and has been used badly. Much has had to be discarded after being tested thoroughly. Moreover, there is a very considerable disagreement among experts on most of these matters even now. Nevertheless, one or two principles are accepted by all intelligent members of the profession. No one will deny that without practice a person learns nothing. It does not follow that a person always learns what he practices, but it is perfectly obvious that unless he is given an opportunity to practice he will learn nothing at all. A second principle of learning which I believe to be axiomatic is that a child or an adult tends to repeat and therefore to practice those acts which bring him satisfaction and by the same token tends to discontinue and therefore not to practice those acts which bring him dissatisfaction.

These two fundamental principles would seem to be singularly simple to apply, but strangely enough this is not the case. We do not realize very often that although we are giving a child practice in a certain thing he may at the same time be practicing something else, and although we try to set up satisfaction or dissatisfaction in connection with a given act, very frequently the child in his mind connects the satisfaction or dissatisfaction with something quite different from that which we intended. A good school invariably will ask itself two questions in any learning situation: "What is the child *really* practicing at this time?" and "With what is he connecting his satisfaction or dissatisfaction?"

In addition to that, a third question always is in the mind of a good teacher in a good school: namely, "What is the motive force which is driving this child in pursuing a given practice or an act?" The principle back of that is also quite obvious: namely, that motives very frequently determine the value of an act. Two people may do the same thing and yet one of them working for a selfish motive will be doing a reprehensible thing and the other, doing exactly the same thing from an altruistic motive, will be doing a highly commendable piece of work. Therefore, it behooves a school to see to it that its children have an opportunity to practice working for high motives rather than for low motives.

If, then, we set up rewards and punishment which are unnatural, the child will begin to work for fear of the punishment or hope of the reward, both of which are low motives. If we artificially create situations which give a child a chance to work for high motives (such as unselfishness and cooperation), we are helping him to practice and therefore to establish the habit which we would like to see in the citizens of the country today. If we artificially set up situations by establishing prizes, which necessarily turn the child away from the motive of working for the sake of the work or because it is of help to his fellows and to mankind in general, and we give him practice in getting satisfaction out of working for a low motive, it then is not surprising if after a while the habit becomes so established that it is not possible for him to act for any other reason except a selfish one or to believe that anyone else can be appealed to on any other ground.

Therefore, a good school gives its pupils every opportunity to practice receiving satisfaction from those acts of life which tend to be useful to the community as a whole: namely, the gratification and contentment that comes to one from being of use to his fellows; the ability to think things through for oneself and arrive at a sensible conclusion, and the gratification one has in knowing that one has contributed to the fund of knowledge of the world, or the comforting feeling that comes to a child when he has found himself able to work his way through his own problem to a satisfactory solution without help.

Unless a school allows a child to make his own mistakes and helps him to interpret those mistakes intelligently, he cannot grow. He merely becomes more dependent upon the adult and less able to cope with the problems of life which lie ahead of him. In this present chaotic state of civilization no adult is able to foretell what type of problem the child will face when he has been graduated from a college even four years hence. Therefore, it is not possible for us to lay down with certainty a curriculum of informational facts and skills which he will find of use upon graduation. We must turn to training him in attitudes toward work, methods of learning, and satisfactions which come from a sense of security and self-confidence and self-respect, together with a faith that in general there is order in this universe, and a law back of nearly everything, which, if we are intelligent enough to discover, we can use for ourselves and our fellows.

It is interesting to note that in the graduate schools and the professional schools you find a very decided turn toward this type of education —just as years ago the kindergarten and primary schools faced the fact squarely and developed a similar attitude. It is in the secondary schools and colleges where the poorest teaching is done today. Therefore, I hope that the pediatricians will concern themselves with the child throughout his growth through the high school years, for it is at that place that so much help is needed. I believe that no one can better give

this than the physicians with whom the child has been familiar since his infancy. In most of the graduate schools courses are being reduced in number; information as such has become more and more unimportant. Such schools as the Yale Medical School, the Dartmouth Business School, and many of the important engineering schools throughout the country constantly are coming back to the center and heart of subjects which they are teaching, leaving the minutiae of information in their subjects to come when the student begins to specialize in his chosen field of work but emphasizing more and more the value of knowing relationships between fundamental principles and ideas.

Dean Doherty, of the Yale School of Engineering, once told me that when he was a member of the staff of the General Electric Company in Schenectedy, N. Y., he was in the habit of taking his problems to Dr. Steinmetz, whose laboratory was not far from his own, and that he became struck with the fact that Dr. Steinmetz helped him to solve his most baffling problems by means of the application of the most simple and elemental principles. One day Dean Doherty says he stopped in the snow between his laboratory and that of the "old man," as they called him, for it came over him that in all the times he had appealed to Dr. Steinmetz for help never once had Dr. Steinmetz told him any new fact which Dean Doherty did not already know. Yet he always had solved the problem. Therefore, it was not new knowledge which the great man could bring to him which made the difference, but new relationships between the old and fundamental principles of his field which he himself had not been able to see. It is with this in mind that the Yale Engineering School has reduced the number of its courses to two principal ones. I have seen an examination administered by that school last year, which consisted of one problem giving two simple principles (such as Boyle's law of the expansion of gases and Newton's law of motion) as the basis on which the entire problem was to be solved and then allowing the students to begin with those two and work out their applications to the case in hand.

I find that the better medical schools, too, are doing the same type of thing. The final examinations are not so much written as they are practical—to see not so much whether the student has a vast fund of information as to see if he can use the information which he has. There certainly is a strong tendency to avoid overspecialization in all professional fields, and particularly in medicine.

The same sort of thing is going on in the schools. A short time ago we tended to divide everything up into subject matter compartments with each subject carefully isolated within its own compartment and each department knowing very little about the others—usually with a supreme contempt for all but its own. This is rapidly changing in the good modern schools. The students are studying problems and not subjects; in the case system developed at the Harvard Law School, the

type of method which is being used everywhere, the student learns about many phases at once. The Institute of Human Relations at Yale is another attempt to move in this direction, but you will notice that these instances all come from professional schools and not from high schools or undergraduate colleges.

The reason for this is, I am confident, that the professional school has had its product tested in the field almost immediately after leaving the school. Hence, failures come back on the school almost at once, whereas the secondary schools and colleges have not been in a position to be tested as ruthlessly and quickly by the old law of survival of the fittest among its students. The time is now at hand when the lack of such a test can no longer excuse an institution for not doing efficient work. Dr. William Palmer, the President of the College of Physicians and Surgeons in New York, told me only last year that one of the greatest difficulties that exists is to find young men who, although having been graduated from a reputable college with excellent records, were able to work by themselves on a problem which had not been analyzed for them. If given an examination which was largely a test of practical ability rather than of information and skill, they complained bitterly that it was not fair. He felt that this was because of the conditioning that they had received in the colleges from which they had been graduated.

Nearly all of the great college presidents have agreed that the real test of a student's fitness to enter college is not so much the information which is retained in his memory as the ability to continue his systematic intellectual growth by himself without a set task and without a taskmaster. Yet these very same colleges have made practically no attempts to measure the extent to which a given student possesses such an essential qualification as this. They do not seem to realize the difference in the attitude of a school toward its pupils from that of a college and professional school toward its students. In grammar school and high school the good schools are doing their best to discover and to develop in every one of their students the most of the possibilities that lie within him. It behooves the schools to bring out of the boy or girl all that it can of these qualities which may prove to be of worth later in his life. At the colleges and professional schools they look at this in a different way; there they are examining the young students to determine whether they have the necessary qualifications which are required in such large quantities for their particular field of endeavor. Somewhere in the freshman and sophomore years of college these two attitudes must find the common meeting point and a transition brought about which is not too abrupt and yet which will be complete. This, I am glad to report, is very rapidly being done, for the colleges now admit (in the more enlightened centers) that the school is not principally a place where a student *prepares* for college but that it is primarily a place

where a child is allowed to *live* and to *grow* and that his life in school is an important and integral part of his whole life and may not be slighted with impunity.

It is during this very interesting phase of the latter part of the child's school life that I feel that the pediatrician can be of great service. It is when the child comes out of the formative period into the middle adolescent period (beginning at about the twelfth year) that he begins to discover his own personality. Here, because of the enormous increase in his physical and nervous faculties, the tremendous sensitiveness to light, sound, and touch increases about tenfold, and he becomes a particularly difficult individual to understand. He is no more like the animal which he has been up to this time than the grub is like the chrysalis, nor is he like the butterfly into which he will develop later if he is allowed to grow properly. Although in the human animal nature does not protect him against the buffets of this hard world as well as in the case of the insect with its cocoon, he is going through prodigious changes in his mental and moral make-up in which he needs understanding and sympathy more than anything else. He certainly should not be expected to behave and conform to the adult pattern for which he is not yet ready. The tragedy of this situation is that the very people who are nearest and dearest to him are the ones who frequently hurt him the most.

It is at this time, I have found from my experience with several hundred young adolescents, that they are seeking a friend and confidant who can help them interpret the hundreds of new and confusing sensations and impressions which come flooding in upon them every day. It is here that he needs the greatest understanding and help. It is here, also, that the parents and the home need assistance in understanding their child and his peculiar actions. No one is more fitted to step into the breach than the pediatrician, who usually possesses the confidence of the family to an abounding degree and who certainly should be able to handle tactfully and sympathetically the child in question. The adjustment to authority, the adjustment to the opposite sex, the adjustment to the realities of the world around him, both social and financial, are all of exceeding difficulty and great importance to him. Particularly today when so many of the old landmarks and guideposts are gone, the advice and counsel of one who knows their past and present but also who is not a blood relation is most eagerly sought and deeply appreciated. Sometimes the child can find such a confidant in a teacher in school; if so, it is well, but I feel sure that a great many more will find it in the doctor who knows the entire family situation so well and also has the great advantage over the teacher and parent of not having to seem to judge or discipline.

Here again I feel that both the school and the doctor can be of inestimable use to each other; no school can possibly handle a child at

any one of his difficult stages, but particularly the one just mentioned, unless it knows fairly thoroughly the conditions at home, information about which the physician is in a position to give. On the other hand, I have seen many serious mistakes made by pediatricians who tried to prescribe for their patients without consulting with the school in any way, when a few moments' conversation with the teacher would have given the doctor information which easily could have prevented the mistake. The teacher's attitude and the doctor's attitude must be alike primarily, and in all good schools they are. Again I find in Dr. Aldrich's pamphlet an excellent example of the attitude to which I refer, for he says that the doctor in working with the child should regard himself more as a gardener who is trying to provide the right conditions for the growth of his plants after studying them carefully to find out the differences between them than as the sculptor who is trying with hammer and chisel to shape a block of marble to his own design. Walter Lippmann once put it in an article in *New Republic*, " 'As the twig is bent so is the tree inclined' may be profoundly true, but it does not tend to make straight trees." Both the physician and the teacher are hoping to bring about trees without bends or curves in them whatsoever, normally straight and upright trees which will be a satisfaction to themselves and a pride to all who have had to do with them.

I feel sure that, if the schools and the doctors would attempt to understand each other more fully, they would find over and over again common points at which they can become of great assistance to each other. Therefore, at the risk of seeming presumptuous, I should like to urge upon the American Academy that they bear in mind at least two objectives in regard to the problem of the schools: first, that they do their best to know and to understand thoroughly the local schools in their community and that they try to judge them from the criteria which I have attempted to outline rather than from the usual points of view of fact gathering and examination marks; second, that they throw their tremendous influence (which cannot be underestimated, for a good pediatrician is literally idolized by his patients in a large percentage of the cases) toward the building and creating of good schools where the principles underlying the school are the same as those in good pediatrics. Dr. Brennemann in his paper read before the Boston section of this society several years ago, in a quotation from Ralph Waldo Emerson, seemed to me to give the crux of the entire matter when he said, "Respect the child, be not too much his parent, trespass not upon his solitude." I feel that this expresses admirably the spirit of a good modern school, and that, since the influence of the pediatrician in any given community is as great as it is, I am confident that if they will throw the weight of this influence in the direction of creating schools with that spirit they could bring about a new generation of good citizens of which this country is so sorely in need during these trying times.

NEW POSSIBILITIES OF A PROGNOSTIC DIAGNOSIS IN TUBERCULOSIS OF CHILDREN

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TUBERCULOSIS is an allergic disease. Thus a deeper knowledge of tuberculosis is to be sought in the analysis of allergy.

Three points have been frequently overlooked in the conception of allergy:[1] first of all allergy is a dynamic conception—it has its development and its course. Second, allergy should by no means signify only the change of *reactivity* under the influence of the allergene. It means also a change of *susceptibility* of the organism toward the stimulating or damaging influence of the allergene.

This last statement, although of capital importance for our approach to the problem of allergy, is unfortunately very difficult to understand. A very simple instance may help us to comprehend the difference between these two groups of factors, which determine allergy and which we have called "reactivity" and "susceptibility."

If one individual is offended by another, the result will equally depend on two groups of factors: (1) The offense will be resented differently by different individuals according to their increased or deteriorated amount of susceptibility toward the offense itself. That is, one and the same offense will hurt one individual more deeply than another. (2) The reaction that the offended will undertake toward his assailant will depend not only on the degree of the feeling of being hurt, but also on the temperament and strength of the offended, and these two factors will determine his reactivity.

Thus allergy as determined by two changing groups of factors can be represented as a curve in a system of coordinates with reactivity as the abscissa and susceptibility as the ordinate. Each point of this curve would be determined by two parameters R and S and represent the actual state of allergy.

Third, in all allergic processes a rôle is played by the general biologic law, frequently proved experimentally, that the reaction of the living organism, provoked by any stimulating agent, induces a change of susceptibility toward the stimulus. This change is bi-phasic: the reaction first increases the susceptibility toward the stimulus; in the further course of the reaction, however, the susceptibility becomes less and less pronounced and finally, if the reactive process has been allowed to run to its end, the susceptibility will be reduced to naught and the living, reacting substance becomes indifferent to the stimulat-

From the Pediatric Department of The John Casimir University.

Lecture delivered on March 19, 1934, at the Lister Institute of Preventive Medicine, London.

ing agent. This state of indifference to stimulation, acquired in the due course of the reactive response I call "adiaphorea" and I believe it plays an intimate rôle in the mechanism of healing (hygiogenesis) of infectious diseases.[2]

TOPOLOGIC SCHEME

These preliminary remarks on our conception of allergy enable me to present to the reader my topologic scheme of tuberculosis.[3] The course of any tuberculous infection can be represented in the above system of coordinates (Fig. 1). When a child comes in contact for the first time with Koch's bacillus, its susceptibility toward the damaging action of this pathogenic agent is so low, that it can be put near the 0-point of the ordinate of susceptibility. Subsequently its reactivity is also very low and near to the 0-point of the abscissa of reactivity.

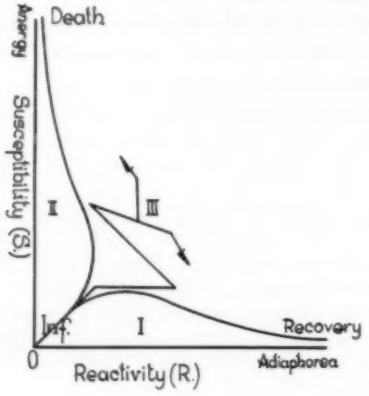

Fig. 1.

The clinical result of this state of affairs is an almost complete lack of symptoms. These will only develop after a certain time, during which allergy develops by synchronous growth both of susceptibility and reactivity. This growth we may assume affects both factors *R* and *S* in an equal degree at the beginning. The allergy is then characterized by an equilibrium between *R* and *S*. Later on three possibilities occur as regards the further development of allergy.

1. The reactivity develops with increased rapidity in comparison with the growth of susceptibility. The effect of this is represented in curve *I* of our scheme. We see that this curve, after a slight initial elevation, representing the slight initial increase of susceptibility, is running along the abscissa and tends to reach the 0-point of the ordinate. It means that susceptibility falls with increasing reactivity toward final healing, represented by a more or less complete adiaphorea. This curve represents those cases of occasional infection which never

develop clinically noticeable symptoms of the disease and heal frequently without the knowledge of the patient.

2. The course of allergy, however, can take an entirely opposite trend. Such course is characterized by an increased and accelerated growth of susceptibility, as shown by curve *II*. This curve runs along the ordinate of susceptibility and expresses reduction of reactivity as susceptibility increases. It tends to meet the 0-point of the abscissa. Here we have an absolute lack of reactivity, which we call "anergy." The susceptibility is at that point infinite, while the reactivity is naught. The ultimate consequence of this course is obviously death. The curve represents those cases of overwhelming infection, which have no time to develop a sufficient amount of reactivity and are from the very beginning heading for ultimate catastrophe.

3. Between these two extreme poles of possibilities oscillates the course of the chronic clinical tuberculosis. Periods of preponderance of reactivity change with periods of preponderating susceptibility, and the final result of the disease depends on the final turn of the curve *III* toward the abscissa or toward the ordinate.

This scheme is purely topologic. In spite of that it can be made very useful in theoretical handling of many problems of tuberculosis and gives a rational basis for a classification of tuberculous manifestations.

METHODS OF DETERMINING FACTORS *R* AND *S* (REACTIVITY AND SUSCEPTIBILITY)

It is obvious that the practical value and importance of my topologic scheme of tuberculosis would be definitely proved if it were possible to determine the factors *R* and *S* in each case of infection and at every stage of its development. The knowledge of these two parameters would enable us first to locate each case of tuberculosis in the *RS* plane of our system at any stage of its development (the *actual state of allergy*) and then to trace and follow up the course of allergy during the period of observation (*the road of allergy*). It is not necessary to emphasize the prognostic importance of such a possibility.

The task of the present experimental investigations, which I undertook in collaboration with my pupil, A. Chwalibogowski, was to find such a method. We thought that a possible estimation of the relationship between the two parameters *R* and *S* might be obtained from the *study of the relationship between the size and the intensity of intradermal tuberculin reactions and the concentration of tuberculin used to provoke them.*

Our experimental method was to inject a different concentration of tuberculin into symmetrical areas of skin of the back of each individual tested and to measure the reactions at the period of their acme in their two largest diameters. The arithmetic mean of these two measurements was considered as the largest average diameter char-

acteristic for the size of the reaction. We had then only to compare our measurements with the concentrations of the tuberculin used to investigate their possible interrelationship.

By this method we were able to detect three different types of relationship between size of intradermal tuberculin reactions and concentration of tuberculin.

1. In the first group of our children with a positive tuberculin test we could observe a marked proportionality between the size of the intradermal tuberculin reactions and the concentration of the tuberculin used. The instance in Table I is typical for this group of children.

TABLE I

No. 55. Name, S—. May 5, 1933.

CONCENTRATION OF TUBERCULIN C.	AVERAGE DIAMETER OF THE INTRADERMAL REACTIONS IN MM. D.	PRODUCT D (–log C)
10^{-4}	18.5	74.0 (= 4 × 18.5)
10^{-5}	14.0	70.0
10^{-6}	12.0	72.0
10^{-7}	10.5	73.5
10^{-8}	9.5	76.0

Table I shows the very interesting phenomenon typical for this group of children, that the diameters of the reactions decrease with falling concentrations of tuberculin in proportion to the negative logarithm of the tuberculin concentration. Consequently, the product of the diameter by the corresponding negative logarithm of the tuberculin concentration is, in each individual of this group, constant. We may at once emphasize that this law proves to be correct only as regards medium intensity of intracutaneous tuberculin reactions and that very strong as well as very weak reactions are to be avoided.

Considering this precise proportionality between the allergic effect and the dose of the allergene as being possible only in cases in which both parameters of allergy, *R* and *S*, remain in mutual equilibrium, we call this category of allergic behavior "homodynamic allergy."

In other groups of tuberculin-positive children the above proportionality is disturbed. Supposing that this is due to an equally disturbed relationship between *R* and *S*, we call such cases "heterodynamic allergy."

Among these heterodynamic cases we can fairly distinguish between two further types.

2. In some children the diameters of the reactions do not decrease with falling concentrations of tuberculin in the expected degree. The reactions continue large. Consequently the product D(–log C) is no longer constant, but increases with falling concentrations of tuberculin. The instance cited in Table II shows this occurrence very clearly.

TABLE II

No. 75. Name, P—. April 29, 1933.

CONCENTRATION OF TUBERCULIN C.	AVERAGE DIAMETER OF THE INTRADERMAL REACTIONS IN MM. D.	PRODUCT D (–log C)
10^{-3}	26.0	78.0 (= 3 × 26)
10^{-4}	22.0	88.0
10^{-5}	20.0	100.0
10^{-6}	19.0	114.0
10^{-7}	17.5	122.5

We consider such cases as being due to a preponderance of susceptibility (S > R) and call them "heterodynamic pleoaesthetic."

3. The third group of children behaves under identical experimental conditions in an exactly reverse way; the diameters drop more quickly than might be expected with change of the tuberculin concentration. The product D(–log C) consequently falls with falling concentrations (see Table III).

TABLE III

No. 2. Name, H—. Nov. 22, 1933.

CONCENTRATION OF TUBERCULIN C.	AVERAGE DIAMETER OF THE INTRADERMAL REACTIONS IN MM. D.	PRODUCT D (–log C)
10^{-3}	20.0	60.0
10^{-4}	13.5	54.0
10^{-5}	8.5	42.5
10^{-6}	6.0	36.0

We consider this kind of heterodynamic allergy as being due to a preponderance of reactivity (R > S) and we call such cases *heterodynamic pleoergic.*

The study of the relationship between the concentration of tuberculin and the size of the intradermal reactions makes possible a differentiation of the tuberculin allergy of the child into the following groups:

1. Homodynamic allergy (R = S)
2. Heterodynamic allergy ($R \gtrless S$)
   a. Pleoaesthetic (S > R)
   b. Pleoergic (R > S).

The above differentiation of the tuberculin allergy in children has been obtained by establishing the behavior of the product D(–log C), which in cases of homodynamic allergy remains constant, falls in pleoergic, and rises in pleoaesthetic allergy, with falling concentrations of tuberculin.

The further question was whether it might not be possible to obtain a notion of the actual dimensions of *R* and *S* from these experimentally

established data of the actual allergic behavior of each case. This part of our work has been carried out with the help of the distinguished mathematician, Professor Hugo Steinhaus, of the University of Lwow.

The actual state of allergy of a case, as demonstrated above, can be represented by the relationship of the diameters of the intradermal tuberculin reactions to the negative logarithm of the concentration of tuberculin. It can thus be expressed by a curve in a plane xy, where x means the negative decimal logarithm of the tuberculin concentration and y the diameter of the reaction in millimeters. By study of these experimentally obtained curves, we have been able to establish the very important biologic fact that all these curves, independently of the category of allergy, can be considered as generalized hyperbolas and expressed by the formula: $y^{\alpha}\ x = \beta$, where x means the negative decimal logarithm of the tuberculin concentration, y the diameter in mm. and α and β are two characteristic parameters. The main feature of such curves is that they appear as straight lines in a plane with logarithmically divided axes. Each such line represents the actual state of allergy of a case and it can be determined by two parameters, which can easily be established both graphically and by calculation. As in cases of simple hyperbolas (e.g., in cases of homodynamic allergy) these two parameters are equal, it was obvious that we can identify them with our theoretical parameters of the actual state of allergy, R and S.

R and S can thus be easily determined from our experimental data if not graphically, with help of the logarithmic paper of Schleicher and Schuell, No. 375½, which is the easiest way, then by means of two observations (x, y, and x_1, y_1) and the following formulas:

$$R = \frac{\log x_1 \cdot \log y_2 - \log x_2 \cdot \log y_1}{\log x_1 - \log x_2}$$

$$S = \frac{\log y_1 \cdot \log x_2 - \log y_2 \cdot \log x_1}{\log y_1 - \log y_2}$$

Nevertheless, this method of establishing R and S might prove too complicated for clinical practice and consequently we worked out very simple charts which permit us to find the exact figures for R and S according to the different values of D at given tuberculin concentrations.

RELATIONSHIP OF TUBERCULIN ALLERGY TO CLINICAL BEHAVIOR

The capital question, whether the above differentiation of tuberculin allergy in children and the estimation of the actual stage of allergy by the determination of R and S have any connection with the clinical behavior, had to be solved on a large series of carefully observed clinical cases; this required a further simplification of our method. It was impossible to perform from four to six intradermal injections in each of our, now over 150, cases to establish their individual and actual state of allergy. We decided, therefore, to employ for this purpose only two injections and to choose such concentrations of tuberculin which, according to our experience, are best adapted for average testing, viz., 10^{-4} and 10^{-6}. Only in cases of exceptionally high or exceptionally low sensitivity to tuberculin (judged from a previously executed von Pirquet test) was it necessary to employ more diluted or concentrated tuberculin solutions, e.g., 10^{-5} and 10^{-7} or 10^{-3} and 10^{-5}.

We thus obtained for our estimation of the actual state of allergy in each case and at the given date, two diameters, D_1 and D_2, corresponding to two concentrations of tuberculin, C_1 and C_2, and could, therefore, establish the category of allergy of the given case first by means of comparing the products: $P_1 = D_1(-\log C_1)$ and $P_2 = D_2(-\log C_2)$. If P_1 was equal or nearly equal P_2, we considered our case as homodynamic; if P_1 was less than P_2, as pleoaesthetic; and if P_1 was greater than P_2, as pleoergic. At the same time we could, with the help of the same data, establish the actual *R* and *S* and thus locate our individual as a point in the plane *RS*, viz., our scheme of allergy.

Besides estimating the actual state of allergy in our cases, we tried to follow them up dynamically. In the majority of our cases we were able to repeat the determination of *R* and *S* several times during a longer period of observation. It was thus possible not only to locate each of our cases as a point in the plane *RS*, but also to follow up its course in time. This course we called the "road to allergy" and consider it as the most important individual feature of the biologic behavior of the organism during the turberculous infection.

RESULTS

The results of our investigations of over 150 cases with over 300 estimations of the actual state of allergy are the following:

To avoid any influence of suggestion we divided our material into four clinically distinct groups. In Group I we summed up all tuberculin-positive cases in which we could not detect any specific symptoms during a longer period of observation (*tuberculous infection without symptoms*).

To Group II belong all the suspected cases without definite symptoms or cases which recently have shown some signs of active tuberculosis, but were actually free from them (tuberculous infection in labile equilibrium).

Group III embraced all manifest cases of tuberculosis with a marked tendency to amelioration and recovery.

Group IV included cases with clinically bad prognosis.

This clinical differentiation of our cases proved to be almost absolutely congruent with our findings of their state of allergy.

Group I proved to belong almost without exception to the pleoergic category of allergy and to hold this position with remarkable tenacity even toward ergotropic nonspecific influences.

Group II belonged almost entirely to the homodynamic category and was particularly susceptible to all specific and nonspecific influences, as proof of its lability.

Groups III and IV were found to belong to the pleoaesthetic category. The difference between them was only of a dynamic character;

they could not be differentiated by means of a single establishment of their actual state of allergy, but their road of allergy is different. While cases of Group III are wandering from the pleoaesthetic zone in the *RS* plane toward the zones of homodynamic and pleoergic behavior, the cases of Group IV take the inverse direction. They are rushing up into still higher regions of pleoaesthesis.

The few exceptions to these rules proved by means of further observation either the superiority of the biologic method over the clinical differentiation or special conditions of allergy, which cannot be detected by our present method.

To the latter kind of exceptions belong in the first place the anergic states of allergy. The final cases of anergy, as for instance, cases of miliary tuberculosis or tuberculous meningitis, behave apparently as pleoergic cases. This is theoretically fully comprehensible. Still more interesting are cases of isolated tertiary tuberculosis. Our present method of valuation of *R* and *S* cannot be applied to adults. Adults with tertiary symptoms behave like pleoergic children. This is due to the fact that the skin of adults is less sensible to tuberculin, thanks to the change in the topography of allergy in the tertiary stage of tuberculosis. This curious behavior of adults is actually the subject of extensive investigations, and we hope to elucidate this problem in the near future. For the present we are not in a position to consider tuberculosis in adults.[4]

CONCLUSIONS

1. The behavior of tuberculin-positive children toward simultaneous intradermal injections of different concentrations of tuberculin (Koch's old tuberculin) is different, and we are able to differentiate three distinct categories of tuberculin allergy in childhood:

a. Homodynamic allergy, in which the product P (= diameter of skin reaction ×–log. of concentration of tuberculin) is individually constant

b. Heterodynamic allergy: Pleoaesthetic—in which P increases as the tuberculin concentration falls

c. Heterodynamic allergy: Pleoergic, in which P falls as the tuberculin concentration falls.

2. The relationship between size of intradermal tuberculin reactions and concentration of tuberculin used is thus characteristic for each individual at the date of investigation and expresses the actual state of individual allergy. It can be represented by a curve in the plane xy where x is the negative logarithm of the tuberculin concentration and y the diameter of the reactions in millimeters.

3. Such curves of the individual state of allergy are generalized hyperbolas and can thus be logarithmically transformed into straight lines. This biologically most important fact permits us to determine

each of these lines—and thus each individual state of actual allergy by the help of two parameters, *R* and *S* (reactivity and susceptibility).

4. A description is given of the methods by which these parameters (*R* and *S*) can be determined.

5. The repeated determination of *R* and *S* during a certain period of observation in the same individual allows one to trace the individual "road of allergy," i.e., the direction taken by the dynamic development of the individual allergy in the *RS* plane.

6. The determination of the actual state of individual allergy and of the individual course of allergy have an important value for prognosis in children. It has been proved on over 150 patients that stabilized and healing tuberculosis belongs to the pleoergic category of allergy, while active cases behave in a pleoaesthetic way. The homodynamic allergy is found in cases in which the state of infection is labile. The following up of the individual road of allergy reveals the prognostic fate of the case: active, pleoaesthetic cases with tendency to amelioration move in the *RS* plane from the pleoaesthetic toward the homodynamic and finally to the pleoergic zone; pleoaesthetic progressing cases wander, on the contrary, to still higher pleoaesthetic regions.

7. Our method cannot be applied to final stages of anergy, and it cannot as yet be used in adults.

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CONGENITAL DISLOCATION OF THE HIP IN INFANCY

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CONGENITAL dislocation of the hip is an important pediatric problem which has been neglected by the pediatrist. This lack of interest often has made necessary a severe treatment of years' duration in cases in which mild treatment of a few months would otherwise be possible. It has made physicians satisfied with a doubtful prognosis when they should expect an excellent one.

The basis for this lack of interest is the failure of diagnosis which is largely due in turn to an anatomical misconception. The term, congenital dislocation of the hip, is a misnomer. The condition present at birth is the absence of a bony acetabulum. There is no congenital dislocation when complications are not present. Dislocation takes place after a force is applied. This force is muscle pull alone in early infancy. Weight bearing increases the dislocation later. That dislocations can take place as a result of trauma, infections, or anomalies is not denied. These complications do not concern us here.

Instruction has been inadequate regarding early signs. It has concerned itself almost exclusively with the dislocation as it exists in children who have started to walk. The general conception has been that the diagnosis was impossible until weight bearing had forced the femora to obvious dislocations. This opinion still prevails despite a few orthopedists' vigorous attempts to correct it. The Freibergs, father and son, of Cincinnati, deserve much credit for their work in this direction. Albert H. Freiberg[1] pioneered in this country for early recognition of the condition. Paci[2] and Lorenz[3] preceded him in the field, but their work was largely with older children. Since these early papers several workers have substantiated their conclusions. Few of these reports have appeared in pediatric journals.

The importance of early diagnosis is apparent when it is realized that abduction for a relatively short time is the only treatment required in early infancy. Freiberg treated his infants with abduction by means of casts. Vittorio Putti,[4] of Bologna, simplified the method by using only splints and massage. The children thus treated were able to walk at the usual age. They had had no reductions and, with Putti's method, no casts.

Furthermore, this condition has been overlooked frequently by the pediatrists on account of its supposed rarity. It is not rare to the

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orthopedic surgeon. In my own pediatric practice I have had four cases in the past two years. This lifts it from the realm of rarity.

That the diagnosis is not difficult, the treatment mild, and the prognosis excellent is illustrated by the following group of infants. One was fourteen months old when she was first seen. She was beginning to walk. The others were diagnosed at two and one-half months, two months, and three weeks of age, respectively. Of these four cases the child on whom the diagnosis was made after she started walking is still under treatment at the end of two years. She has had continuous casts, three closed reductions, and recently open reduction was performed. The others, diagnosed in early infancy, required only splinting and massage. The first of these, diagnosed at two and one-half months, had a bilateral "dislocation." She was clinically normal at eight months. X-ray examination at that time showed beginning ossification of the acetabuli. Treatment was discontinued as the family fled to escape an epidemic. While the child was away from our care, she began standing. Subsequent x-ray plates showed continued improvement until a final one at the age of eighteen months disclosed normal acetabuli. The second, diagnosed at two months, had a left-sided, unilateral, delayed acetabular ossification. When she was four months old, Dr. Ralph S. Bromer, of the Children's Hospital, reported on her x-ray plates as follows: "There has been excellent development of the left acetabulum so that now it is approximately the same as the right. It seems to me that a diagnosis of potential dislocation is no longer warranted." Treatment of the third, through a misunderstanding, was delayed until she was three months of age. Now, at six months, she is still under treatment but her progress has been excellent, and a cure is anticipated by eight months. Diagnosis was substantiated and progress checked by stereoscopic x-ray examination in all cases. These patients were treated by Dr. Varnum Southworth, orthopedic surgeon, to whom I am greatly indebted for his invaluable cooperation. There has been only one child on whom the diagnosis was mistaken when the physical signs seemed to warrant an x-ray examination. Even in this case the hip was not normal. Dr. Henry K. Pancoast, of the University Hospital, reported "fullness of the periarticular soft tissue structures" on the affected side.

Frequency of Occurrence.—This cannot be accurately estimated. In the past ten years the Children's Hospital of Philadelphia has admitted thirty cases. This gives no index to its frequency because it is solely a treatment of election. Mention is made of the number admitted simply as evidence that it is not unusual. Orthopedic wards are seldom without a case. All the patients in the Children's Hospital, with one exception, were girls. Two were sisters, identical twins. The family incidence was not studied. Most workers believe it occurs as a hereditary trait. During the same ten-year period the Children's Hospital had only ten

diabetic patients. Diabetes is not considered rare, and a higher percentage of its victims must necessarily reach hospitals.

Etiology.—The explanation for delayed ossification of the acetabulum can be only conjectured. It does not seem to be a defect in development. There are two reasons for believing this.

First, it is rarely associated with other defects. Twenty-nine of the above mentioned children were otherwise normal. It may be significant that the thirtieth child was the only male of the series.

Second, the acetabulum forms normally when the head of the femur is held in its proper position. Wolff's law, regarding the changing of a bone's internal structure by its external stresses and strains, may explain the delay. Normally there is muscle pull forcing the head of the femur into the acetabulum. Without this pressure there would appear to be no incentive for ossification of the acetabulum. That it is formed in cartilage we can hardly doubt, as it develops embryologically by the time the fetus is from 20 to 25 mm. in length.[5] It is conceivable that the force may be changed in direction at times so that it be away from the pelvis. A fulcrum between the hip and the knee in the fetus would cause such a reversal of force. Uterine pressure upon the knee would then spring the hip from its socket. The fulcrum might be formed by the crossing of the legs, by an arm between the abdomen and thigh, but more likely by a wide pelvic crest. Additional evidence favoring this hypothesis is the fact that it occurs so predominantly in the female with the wider pelvis. Joseph A. Freiberg reached a somewhat similar conclusion. Familial tendency can be explained by the inheritance of wide pelves or characteristic postures in utero.

Diagnosis.—A correct anatomical concept is essential to an understanding of the condition. With this in mind the signs become logical.

At birth, as stated above, there is no bony acetabular formation. This leaves the head of the femur unanchored. Muscle splinting is required for stabilization. It is analogous to a fracture in this respect. All the muscles from the pelvis to the femur take part in the maneuver. Even the hamstrings to the leg assist. When the thigh is in a straight line with the body, the insertions of these muscles are below the femoral head with origins, on the pelvis, well above the insertions (Fig. 1). Hence in this position they unite in an upward pull. Great distortion is not likely, however, because of the medial origins of the muscles. Only the small group of abductors do not arise medially to the head. The bony structure is well designed to impede upward dislocation. The flat ilium slopes outward as it arises. This inclined plane helps to hold the femoral head in its intended place. Eventual fatigue or stretch of the adductors permits gradual dislocation of the femur. Such dislocation is a slow process. Weight bearing greatly speeds the displacement.

By reviewing the anatomic structures around the hip joint, the signs can be anticipated. In a child with this condition the adductor group will be the most affected by any sliding of the femur in a lateral direction. The pectineus, adductor brevis, and the upper fibers of the adductor magnus are immediately put on stretch by such a movement. To a lesser degree the gemelli, quadratus femoris and the obturators would resist the motion. The abductors, pulling from above, would be much less intimately affected.

Inasmuch as the adductors are also external rotators, stretch causes an outward rolling of the thigh. This will be directly proportional to the extent of lateral displacement.

Upward dislocation shortens the extensors and flexors of the thigh. The flexors are less completely contracted than the extensors because of their greater length. Allowance for the shortening of the hamstrings is made by flexion of the foreleg.

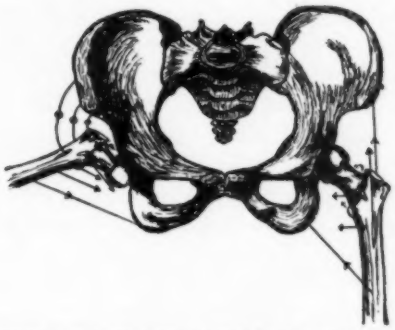

Fig. 1.—Diagrammatic representation of the muscle pull from a normal pelvis to femur. Muscles from both posterior and anterior aspects of the thigh are represented. The left side illustrates the femur in direct line with the pelvis. The right side shows the femur in abduction.

In recapitulation then, we find the femur relatively immobilized by all its muscles. There is a definite spasticity of the adductors. These are often the only signs present in early infancy. As the infant grows in strength, the upward muscle pull increases the displacement and the external rotation becomes more marked. The thigh is held in almost constant flexion and the leg may resist extension.

Now let us look at a young infant with a unilateral delay of ossification of the acetabulum. The mother has noticed nothing abnormal. It lies on its back and is symptom-free. Both legs are drawn up comfortably. It kicks freely with one leg while the other is held motionless. The child appears so well it is difficult to believe that only one leg is being used.

On extending both legs flat to the table one may meet with resistance on the affected side. When the legs are thus extended a somewhat

higher inguinal fold is noticed on this side producing a more acutely angulated crease (Fig. 2). One must be sure that the legs are straight, as distortion is easy. The gluteal fold, also, is a little higher. This may produce an asymmetry of the lower spinal region which can be easily mistaken for a scoliosis. This is more satisfactorily demonstrated by setting the child up. In this position it will be seen that the buttocks are not equal. The creases in the backs of the knees are similarly asymmetrical. At the ankles the same is true. Conceivably, in bilateral cases this asymmetry might not exist. Practically, the two sides are not apt

Fig. 2.—A. Posterior view of an infant with delayed ossification of the acetabulum on the right side. Dislocation is beginning. The asymmetry of the gluteal and knee folds is shown. Note the fold on the mesial aspect of the right thigh. This may or may not be present. See text.

B. Anterior view showing the angulation of the right inguinal fold. External rotation is present.

C. Demonstration of the limitation of abduction on the right side.

to be entirely identical in degree. Other folds are usually unimportant. For instance, there may be markedly asymmetrical creases on the medial aspects of the thighs (Fig. 2). There may be none on one side or a discrepancy in number. Although a difference occurs at times in this condition, it occurs in a high percentage of normal infants as well. It seems to have little significance but is always worthy of investigation as to cause.

When the knee is raised to right angles with the body, abduction in this position should be normally 75 to 90 degrees from the perpendicular. On the affected side it will be 45 degrees or less.

When any or all of these findings are present, an x-ray examination is warranted. Incidentally, x-ray plates of delayed acetabular ossification are not frequently taken. On this account the roentgenologist is likely, with all respect to him, to be as inexperienced as the pediatrist in this condition. The plate shows, as we expected, no bony acetabular formation and little or no displacement of the head of the femur. The ilium is not angulated preparatory to the formation of a future acetabulum as it is normally, but is flat or even concave on the surface facing the femoral head. The epiphyseal center of the head is sometimes rather larger on the affected side. Its outline is irregularly ovoid as against the even circle of the normal center. Only in very early infancy is this true. As the epiphyses develop, the normal side grows much faster, while ossification is slow on the affected side. Bony acetabular formation, even at birth, is normally evident to x-ray examination.

The signs usually expected are not encountered in these early cases. There is no obvious widening of the perineum, no absence of the head of the femur from its proper site, and no widening of the pelvis. These signs do not develop until later.

Treatment.—On this subject there are two schools of thought. One, the conservative, believes in early treatment. This takes advantage of the period of rapid bone formation. As there is no displacement to overcome at this age, only splinting is necessary. Details of this treatment will follow. The second, or radical school, believes in allowing the child to develop physically to the point of more solid bone formation before therapy is begun. When this age is reached, traction is applied to overcome the dislocation caused by walking and long-continued muscle pull. Closed or open reduction, and often both, follow it. For this group early diagnosis is nonessential.

The anatomic explanation for the success of the conservative treatment is as follows: When the thigh is held in a straight line with the body, there is an upward pull from all the pelvis-attached muscles. This is not the case when the thigh is in abduction. The muscles then have a medial pull (Fig. 1). The origins of the muscles on stretch in this position are horizontal to, or below, their insertions in the thigh. Those whose origins are higher than their insertions are relaxed. The abductors are passively contracted beyond use, but, if they pull at all, they will pull medially. The force of the pull is medial and downward. When this direction of force is applied, the head is guided into its intended place by the small muscles surrounding it, the obturators and the gemelli.

Putti took advantage of these anatomical facts when he began splinting the thighs in abduction. His apparatus is of two kinds. One con-

sists of boards strapped on the inner surfaces of the thighs and hinged together at the perineum. The amount of abduction is controlled by an umbrella-staff arrangement with a setscrew. His other is a cushion, triangular in shape, with straps on two sides to be secured in a similar manner to the inner aspects of the thighs. Other orthopedists have devised apparatus equally simple in nature. C. H. Jaeger,[6] in his method, uses pressure pads above the head of the femur to ensure its descent into the acetabulum. Joseph A. Freiberg[7] has an ingenious method of accomplishing the same effect. He uses individual casts, one on each leg to the mid-thigh. Between the ankles is a turnbuckle to control the abduction and to form a fulcrum on which a turnbuckle between the knees pulls in adduction. M. Forrester-Brown[8] uses metal splints on the external aspects of the thighs. These are hinged to similar strips

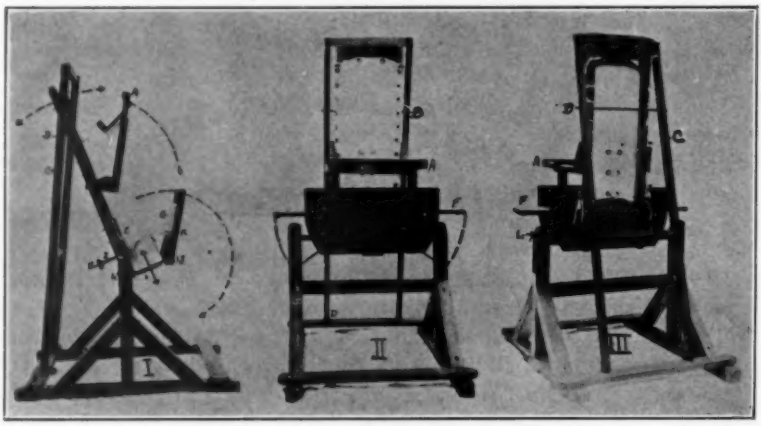

Fig. 3.—Chair-bed abducation apparatus.

I. Lateral aspect with the arcs of variations in dotted lines:

A, feeding tray; *B*, crossbar. This can be removed and inserted into holes seen lower on back-rest. *C*, back-rest. This is hinged at *D*. *F*, Putti type of abduction splint. It is built in two halves hinged in the middle at *E*. Each side is adjustable to the desired angle where it is held by the removable peg, *K*, *G*, Anterior plate, hinged at the bottom. It is secured in the upright position by hook, *J*. This slips over the end of bolt, *H*. The tension spring, *I*, permits the anterior plate to have a little forward motion. The entire apparatus can be inclined on the axis, *L*, to any angle from vertical to horizontal.

II. Anterior aspect of the chair-bed in the upright position. The possible variation of angle of the abduction splint, *F*, is shown in diagrammatic lines.

III. Posterolateral aspect. Note holes through both posterior and anterior plates for the pegs which hold the adjustable splint. The posterior plate is cut away, inside the back frame, to the level of the splint. This allows room for the buttocks. The canvas back is of Bradford frame dimensions.

strapped to the sides of the body. This apparatus has the advantage of simplifying excretory hygiene.

These methods of treatment require the recumbent position. This is the comfortable and logical posture for infants under six months of age. At approximately this age a normal child begins to sit up. Those with delayed ossification of their acetabuli, being normal otherwise, at-

tempt it. Frustrated by the apparatus, they become fretful and irritable. There is no contraindication to the sitting posture so long as abduction can be maintained. This position has an advantage over the recumbent posture because the weight of the child can be utilized in

Fig. 4.—Patient A. C. C., aged two and one-half months; bilateral delay of ossification of acetabuli.

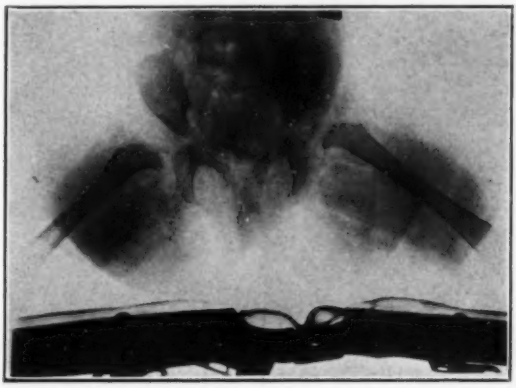

Fig. 5.—Patient A. C. C., aged four months. Plate shows good position of femoral heads with abduction alone. No reduction was necessary.

forcing abduction. With this object in mind a chairlike apparatus was built. In it is incorporated an adjustable Putti abduction splint as a seat. The back is similar to a Bradford frame in shape and dimensions with canvas stretched over its uprights. Anterior and posterior to the

Fig. 6.

Fig. 7.

Fig. 6.—Patient A. C. C., aged eighteen months.

Fig. 7.—Patient J. W., aged three weeks; delay of acetabular formation on right side.

Fig. 8.

Fig. 9.

Fig. 8.—Patient A. W., aged two months. Note that the epiphyseal center of the femoral head is larger and less dense on the affected side than on the normal. Its shape is irregularly ovoid as against the even circle of the normal.

Fig. 9.—Patient A. W., aged four months. Note great improvement in acetabular ossification.

splint are retaining plates to keep the legs in position. The anterior is hinged at the bottom and held parallel to the posterior one by an adjustable tension spring. This permits occasional bending of the knees but the spring pressure soon tires the leg and forces it straight again. A second advantage in the hinging of the anterior plate lies in the fact that it can be swung out of the way to facilitate seating and removing the baby, thus allowing the infant to be readily lifted out for the changing of diapers. There are no straps and buckles for the mother or nurse to struggle with. For feeding and amusement purposes a tray similar to those on high chairs was added. The entire apparatus can be inclined on its base and held at any angle, thus forming a chair by day and a bed by night. The infant may sit, lounge, lie prone or supine as seems the most comfortable. This apparatus allows the child to lead a normal life while undergoing treatment.

SUMMARY

1. We believe there is no dislocation of the hip at birth except in the presence of complications. There is, instead, a delay in bony acetabular formation.

2. A plea is made that pediatrists consider the early recognition of this condition as their problem.

3. The relative frequency of its occurrence is emphasized.

4. The signs on which the diagnosis should be suspected are reviewed and explained anatomically.

5. A new apparatus for abduction therapy is described.

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GREENE AND COULTER STREETS

PHYSICAL MEASUREMENT AND NUTRITIONAL STATUS

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THE weight for height tables stimulated great interest in malnutrition of school children for many years. But the assumption that these tables could be used as a valuable index of nutritional status has interfered with sound clinical procedure in the selection of undernourished children in many schools. A knowledge of the factors which influence the weight of school age children has shown that weight for height is more nearly an indication of certain kinds of skeletal build than of nutritional status.[1]

The new ACH. index of nutritional status[2] should revive interest in malnutrition of school children because of its economy in eliminating the many cases that are most likely to be well nourished,[3] and therefore allowing more time to be given to school physical examinations of a small group of children containing a high proportion with poor nutrition. The American Child Health Association has recently published tables[4] for an evaluation of three physical signs of nutritional status that the writer has used in school examinations during the past year. As this experience has indicated various applications of these measurements, several cases are presented with a discussion of their interpretation in the interest of further study and testing of the new measurements on an extensive scale.

Table I gives the status of eight children in three physical signs of nutritional status. They were referred by teachers for special examination for various causes including suspected malnutrition. In the opinion of the writer they are representative of some of the various types of poorly nourished children found in public schools in need of medical health supervision. The figures for each measurement for a particular child show the number in 1,000 of his or her peers who are lower in the given measurement than the particular child. The 1,000 peers used for comparison with each case are representative of children of the same age and sex having the same combination of height, hip, chest breadth, and chest depth dimensions.

The first two children, Ruth and James, are quite obviously undernourished children. Both are much underweight for their build. In a random 1,000 eleven-year-old girls with the same combination of height, hip, chest breadth, and chest depth dimensions, only eleven children, or 1 per cent, would be found who did not weigh more than Ruth. Among seven-year-old boys with the same four skeletal dimensions as James, only twenty would weigh less. They are both children with small mus-

culature when compared with their skeletal peers. Ruth's musculature is so small that a smaller arm girth would be found not more than seven times in a random 1,000 girls eleven years old with the same skeletal

TABLE I

STATUS DISTINCTIONS OF CHILDREN IN WEIGHT, ARM GIRTH, AND SUBCUTANEOUS TISSUE COMPARED WITH THEIR PEERS IN BODY BUILD

NAME	AGE	SEX	STATUS DISTINCTIONS. NUMBER IN 1,000 LOWER THAN EACH CHILD*			ACTUAL HEIGHT INCHES	ACTUAL WEIGHT POUNDS	AV. LB. WT. FOR HEIGHT†	POUNDS WT. FOR BUILD‡
			WEIGHT	ARM GIRTH	SUBCUTANEOUS TISSUE				
Ruth	11	F	11	7	60	51	53	63	65
James	7	M	20	60	200	47	43	50	49.2
Georgiana	9	F	55	159	44	50¾	56¾	61	63½
Shirley	9	F	14	270	80	54½	68½	70	77½
George	8	M	40	212	250	50½	58½	58	64½
Edward	7	M	68	90	500	48¼	47½	53	52
Rose	9	F	55	98	120	49½	57½	55	64½
Frances	8	F	65	105	450	49½	55½	55	61½

*The figures for each measurement for a particular child show the number in 1,000 of his or her peers who are lower in the given measurement than the particular child. The 1,000 peers used for comparison with each case are representative of children of the same age and sex having the same combination of height, hips, chest breadth, and chest depth dimensions.

†Compared with Baldwin-Wood tables.

‡Compared with peers of the same height, hips, chest breadth, and chest depth dimensions.

dimensions, and only 60, or 6 per cent, would have as small arm girth as James among his peers. They are also low in the amount of subcutaneous tissue as measured by the thickness of the skin fold over the biceps with special subcutaneous tissue calipers.[5] This measurement on Ruth indicates only 60, or 6 per cent, out of 1,000 girls of the same age and with the same skeletal dimensions would have a smaller amount of subcutaneous tissue, and 200 boys, or 20 per cent, would have as small an amount as James.

Both of these children are well below average for their age and sex in all four skeletal dimensions. Even with average weight, musculature, and adiposity, children with such slender frames are likely to give the impression of thinness. These children are so unusually low in all three physical signs that they appear thin and frail and suggest poor nutrition to the casual observer. The clinical examination also shows very little flesh over the chest, well-defined winged scapulae, and soft flabby muscles.

The third child, Georgiana, has about average skeletal proportions and is not so obviously underdeveloped in musculature and adipose tissue.

Her measurements, however, indicate she is sufficiently underweight for her skeletal dimensions and with arm girth and amount of subcutaneous tissue so unusually low that further inquiry regarding her nutritional status is advisable. Only fifty-five in a random 1,000 of her peers in skeletal dimensions would weigh as little as she, and only 159 in 1,000 would have smaller arm girth and forty-four would have a smaller amount of subcutaneous tissue. According to the Baldwin-Wood tables, average weight would be 61 pounds, while average weight for nine-year-old girls with her skeletal dimensions is 63½ pounds. Although we have said Georgiana has about average skeletal proportions, actually she is about 1 inch below average height and slightly below in chest breadth, chest depth, and hip dimensions, which fact accounts for an average weight for build which is 2½ pounds above the average for the tables based on height. While the difference in this case seems to be small between the average weight for the Baldwin-Wood tables and the average for four skeletal dimensions, we may explain that her biologic position as indicated by 55 in 1,000 is unusual because variations in weight of school age children is very largely influenced by the skeletal dimensions, and there is generally little variation from the average weight derived from four skeletal dimensions.

It may be seen that the fourth child, Shirley, is very low in weight for build and low in amount of subcutaneous tissue, but she has an arm girth somewhat better than the previously mentioned children. This girl has badly infected tonsils with recurrent tonsillitis and acute cervical adenitis; she failed to gain weight during our three-month period of observation. Other evidences of malnutrition in this case are limited energy and rather feeble endurance. We might expect to see a satisfactory gain with the removal of this foci of infection.

George, the fifth child, is very much underweight for his build but less underdeveloped in musculature and adipose tissue than the other children. He has a fair musculature over the chest and in no way appears emaciated. He is a rather large boy for his age being above average in height, both chest dimensions, and hips. His mother reported that he had no appetite for breakfast and asked that he have a mid-morning milk lunch in school. It seems quite possible that this boy may have had a spurt of skeletal growth which accounted for his underweight and small sized musculature and adiposity in proportion to his frame. Four months later he had gained four pounds, and his arm girth was average for his build.

Edward's weight and his musculature status is very low, and his subcutaneous tissue is average for his build. He is of about average height with about average chest breadth and a shallow chest and narrow hips. Both arms and legs appear very thin, and his muscles are very soft and flabby. This child is one of nine children. The family is entirely dependent on public relief; investigation shows a diet of excess starchy

foods which may account for his adipose tissue. During six months' observation he gained only ½ pound.

Rose is low in all three physical signs although she is 2½ pounds above average weight for her height. She has been a preventorium patient because of hilum tubercular infection. When first examined, she gave the impression of having a well-developed musculature because she is short and has an unusually broad and deep chest with average width hips. This kind of frame is difficult to judge without measurement and the greater weight, musculature, and adipose tissue appropriate for her frame was not readily appreciated without the tables for comparing her measurements. Her poor development was more apparent six months later when because of poor home conditions she had not gained in weight, and she had gained 1 inch in height. Then her posture definitely indicated her poor muscle tone, and the depressed intercostal spaces emphasized a thin chest.

Frances is another child of average weight for height, but she is underweight and with undersized musculature for her stocky frame. She is average height and above average in chest breadth, more than one sigma above average in chest depth, and above average in hip width. Her nearly average amount of subcutaneous tissue is probably due to a diet of excess starch and sweets. She has very badly decayed teeth and lives under very poor home conditions.

These measurements compared with a random 1,000 children of the same skeletal build are not in themselves an evaluation of nutritional status, but they do give reliable, objective, and valid distinctions in weight, musculature, and adiposity which are significant in such an appraisal. They are indices of physical signs which should be properly evaluated in a composite of signs and symptoms. Of course, deviations from an average should not be interpreted directly as desirable and undesirable signs, but the average provides a convenient reference point which gives definiteness to the measurements. The use of accurate distinctions in these three physical signs releases the clinician from the difficulties of individual judgment and gives him greater freedom to apply all the subtleties of the art of medicine in judging function, growth, and development and all the intricate factors involved in the nutritional process.

The appraisal of the nutritional status as a basis for health supervision requires a consideration of the whole child, his social setting, and the coordination of many factors which may influence his well-being. But so far as reliance is placed upon the evaluation of physical signs observable at any one time, it is important that this evidence be dependable. The pediatrician evaluates muscular development and adiposity every day in his clinical appraisal of nutritional status. He generally considers the weight to determine the over-all growth but he recognizes the

need for improved criteria in order that he may interpret properly the individual differences in weight. Any general conclusion about the muscular development must be built up from estimates of various muscles or groups of muscles. Such estimates, of course, are difficult to make accurately without measurements and standards. This is especially true because the size of the skeletal framework influences so much the size of the muscles and allowance cannot be made for the type of build since children do not readily fall into types of skeletal proportions but present all possible kinds of combinations of chest breadth and depth, height, and hips. This is shown by some of the cases presented above.

Malnutrition has been regarded by some as a clinical entity.[6] Then the diagnosis presumes the recognition of a well-defined syndrome. Of course, the occasional case may be found which presents a clinical picture very similar to the textbook description of malnutrition. In most cases, however, the picture is blurred by a variation in the degree to which the signs and symptoms are clearly recognizable. Good nutrition and malnutrition are obviously the extremes of a scale. The significant signs and symptoms are variable rather than categorical distinctions. While malnutrition may be a useful term to designate extreme cases, the pediatrician who would give advice and guidance relative to nutrition cannot afford to limit his service to the typical cases of malnutrition.

Such a definite appraisal of three morphologic factors raises questions of the share of immediate and remote influences that are responsible for changes in musculature, adiposity, and over-all growth as revealed by weight. The gain or loss in weight may continue to be our most satisfactory measurement for children followed over a period of time, but the measurement of these important physical signs is, in the experience of the writer, most valuable in evaluating nutritional status of the children seen for the first time because it contributes evidence that is free from personal judgment. It seems reasonable to expect that further study of our cases with the help of these measurements may reveal that diet, excess fatigue, foci of infection, or other etiologic factors may show rather immediate manifestations in muscular development or in the limitation of subcutaneous fat. Deficiencies in function such as digestive disturbances, nervousness, hyperirritability, overactivity, restlessness, and anorexia may be findings which may possibly be associated with certain kinds of development. The secondary anemia, the soft and flabby muscles, the poor circulation, and limited energy or definitely feeble endurance are the kind of advanced manifestations of malnutrition which we should like to prevent. One of the handicaps we have labored under in the prevention of malnutrition has been our limitations in the evaluation of physical signs of the more or less well child. Precisely measured physical signs should help to overcome this handicap and offer further prospect of recognition of premonitory signs of malnutrition.

SUMMARY

Numerical distinctions in weight, musculature, and subcutaneous tissue are reported for eight children with proper allowance made for differences in four skeletal dimensions.

These distinctions are presented as objective and valid physical signs of nutritional status. The interpretation of these physical signs is discussed. Deviations from an average in indices of physical signs is interpreted as a valuable aid in the appraisal of nutritional status at any one time. A proper evaluation of these three physical signs in a composite of all signs and symptoms is proposed as a possible means of a better understanding of the nutritional process and of determining premonitory signs of malnutrition.

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BRAIN TUMORS IN CHILDHOOD

Review of Thirty-Eight Cases

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FROM the standpoint of the pediatrician the diagnosis of intracranial tumors has a practical clinical application. It is not necessary to have a highly specialized neurologic training in order to arrive at a tentative diagnosis of brain tumor. Too frequently, however, in dealing with children, the possibility of such a lesion is not given sufficient regard. In reviewing our charts we found evidence that not infrequently brain tumor was a late, rather than an early, consideration. In this presentation the authors make no effort toward fine neurologic distinctions. Emphasis will be placed on the more obvious signs and symptoms encountered in children suffering from intracranial tumors.

This report is based on a series of verified and suspected brain tumors in children who were admitted to the Children's Hospital of Los Angeles from Jan. 1, 1924, to May 1, 1934. During this decade there were 11,340 admissions to the medical service. Our group comprises thirty-eight cases, giving a ratio of 0.335 per cent, or one brain tumor in every 298.6 medical admissions. None of these children had reached the thirteenth birthday.

It has been estimated by Williams[1] that brain tumors in general represent about 1.8 per cent of all tumors of the body. Brain tumors are said to be relatively less frequent in children than in adults; Cushing[2] giving the ratio of approximately one tumor in childhood to six in adult life. Certain types of tumors frequently seen in adults, i.e., meningiomas, acoustic neuromas, and pituitary adenomas, seldom if ever occur in children under twelve years of age. The proportion of gliomas in children is therefore increased and is approximately 75 per cent of all intracranial tumors, while in adults the percentage would range from 37 per cent to 42 per cent. Cushing raises the question whether or not many more brain tumors go unrecognized in children than in adults. The majority of these are various types of gliomas with an occasional tuberculoma and rarely a congenital cystic tumor. The cerebellum is the seat of predilection for gliomas in children. Cushing gives the ratio of cerebellar to cerebral tumors as 2 to 1 in children; as compared to 1 to 5 in adults.

In this study we have considered tuberculomas in the category of tumors because it is difficult to distinguish between the two types of lesions clinically. Tuberculomas are said by Bailey[3] to be "four times

as frequent in children as in adults." They are, however, relatively infrequent as compared to gliomas even in children (ratio 1 to 10) and rarely occur in adults. When present in children, tuberculomas are said to occur more frequently in the cerebellum. This was also our experience, as out of three cases two were in the cerebellum and one in the right parietal lobe. The tuberculomas represented 7.8 per cent of the entire series. All were in Mexican children.

Of this group of thirty-eight tumors (Table I), eighteen have been verified as some type of glioma either by operation or autopsy, three as tuberculomas, and one as a Rathke's pouch cyst, and one as a cholesteatoma. In fifteen not verified by tissue study, the diagnosis

TABLE I

TYPES OF TUMORS

Gliomas (verified)	18
Gliomas (probable but not verified)*	15
Tuberculomas (verified)	3
Rathke's pouch cyst (verified)	1
Cholesteatoma (verified)	1
Gummas	0
Total	38

*These fifteen cases not verified by tissue study were in all probability gliomas of some type.

of brain tumor is considered as highly probable. There was no gumma in this series, and in only one instance was there a positive blood Wassermann reaction in which a verified glioma (probable medulloblastoma of the fourth ventricle) existed. The cerebrospinal fluid Wassermann reaction in this case was negative. This bears out the well-known fact that cerebral gummas are very rare and that gliomas may develop in syphilitic patients.

The cases of both verified (Table II) and unverified but probable tumors (Table III) have been grouped according to the general location of the growth. Approximately two-thirds of the verified tumors, 69.5 per cent, and a majority of the unverified tumors, 60 per cent,

TABLE II

LOCATION OF VERIFIED TUMORS*

Rathke's pouch cyst	1
Third ventricle	2
Right cerebral hemisphere	4
Left cerebral hemisphere	0
Midbrain	0
Fourth ventricle	8
Right cerebellar lobe	2
Left cerebellar lobe	1
Cerebellum (bilateral)	2
Medulla	1
Vermis	2
Unlocalized	0
Total	23

*Of these, 69.5 per cent were subtentorial.

were subtentorial. The majority of these posterior fossa lesions were either in the fourth ventricle or in some portion of the cerebellum. The ratio of subtentorial to supratentorial tumors in the verified group was approximately 7 to 3, while in the unverified group the ratio was 3 to 2 making the proportion of cerebellar, as compared to cerebral, lesions in our series somewhat greater than the established figures.

TABLE III

CLINICAL LOCATION OF UNVERIFIED TUMORS*

Rathke's pouch cyst	1
Third ventricle	2
Right cerebral hemisphere	1
Left cerebral hemisphere	0
Midbrain	2
Fourth ventricle	2
Right cerebellar lobe	2
Left cerebellar lobe	1
Cerebellum (bilateral)	2
Medulla	0
Vermis	0
Unlocalized	2
Total	15

*Of these, 60 per cent were subtentorial.

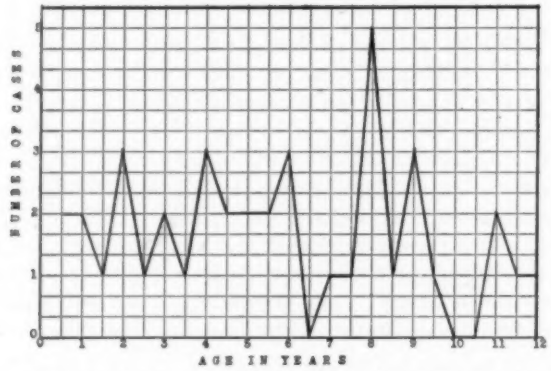

Chart 1.—Graph showing the relative frequency of tumors at various ages. The greatest number occurred at eight years of age. The others showed no predilection for any particular age.

AGE OF INCIDENCE (CHART 1)

In considering the age incidence, one is immediately impressed by the fact that early age is not an argument against the possibility of the presence of a brain tumor. The youngest patient was an infant of ten months on whom a diagnosis of encephalitis had been made. The spinal fluid contained thirty-three cells and increased globulin and was under increased pressure. An intracranial tumor was not suspected, but upon autopsy multiple gliomas of the cerebellum with spontaneous hemorrhages were found. The next youngest child,

eleven months old, had a fourth ventricle tumor, probably a medulloblastoma. The discs were not choked. The spinal fluid in this instance was under increased pressure, contained no cells, and gave a negative globulin test. There was paralysis of the right third and sixth cranial nerves, accompanied by hydrocephalus and convulsions. The greatest number of tumors, five in all, occurred in an eight-year-old child. The remaining thirty-one cases showed no predilection for any age but were scattered over an age period from one to twelve years.

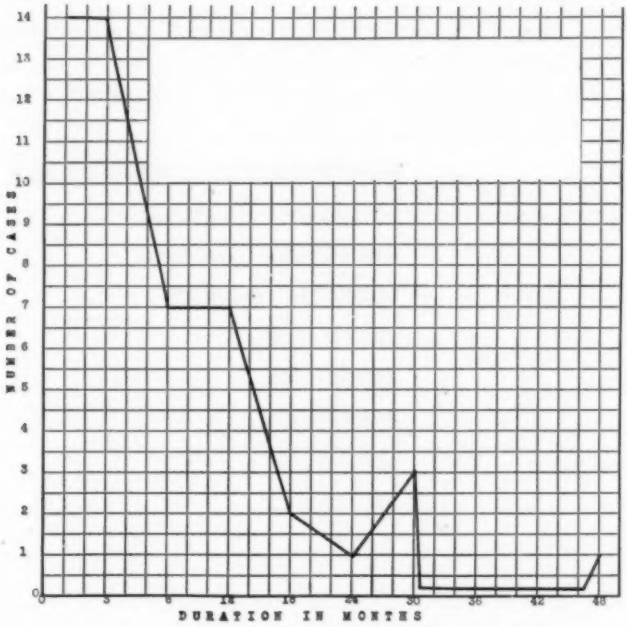

Chart 2.—Graph showing duration of symptoms in months before admission. All patients had symptoms one month or more before being seen. Three patients not included in this graph had symptoms five, eight, and five years, respectively, before being seen. One of these was a cystic glioma; the other two, cystic congenital tumors.

DURATION OF SYMPTOMS IN MONTHS BEFORE ADMISSION (CHART 2)

If one is confronted with a child who has been sick only a few hours, or possibly days, the probability of a brain tumor is remote. This is well brought out in Chart 2. Fourteen of the children had symptoms for at least from one to three months before admission. Fourteen additional cases showed symptoms from six months to a year previous to hospitalization. Two patients had symptoms for eighteen months; one, for two years; three, for two and one-half years; and one, for four years before admission. Three additional cases were not included

in this graph because their symptoms had covered a period of years rather than months, being five, eight, and five years, respectively. One of these was a cystic tumor of the vermis (probably an astrocytoma); the second was a suprasellar (Rathke's pouch) cyst; the third was a cholesteatoma in the neighborhood of the optic chiasm, invading the third ventricle. In other words, the first of these last three cases was cystic; the other two were both cystic and congenital. All of these conditions would imply slow growth and bespeak a relatively long prodromal period.

RELATIVE FREQUENCY OF PRESENTING SYMPTOMS (CHART 3)

The time element does not preclude the possibility that the physician may be confronted with an acute emergency in a child suffering from a brain tumor. The parents may give a history which on the surface

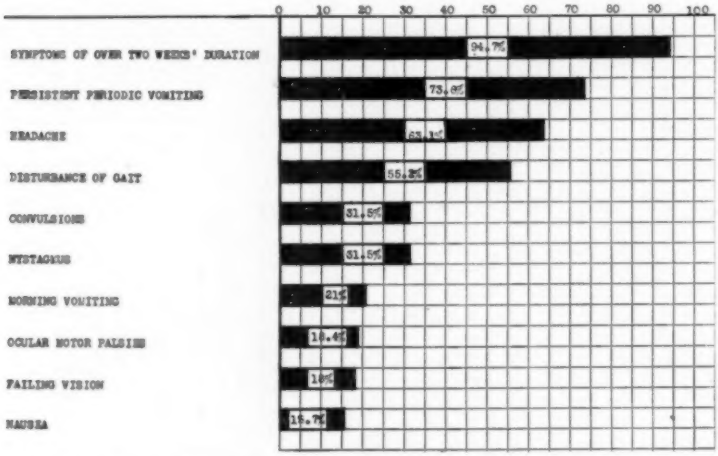

Chart 3.—Graph showing relative frequency of principal presenting symptoms.

would seem to point to a short illness overlooking symptoms which go back over a period of time. These symptoms may have seemed to them to be of little significance but in reality are of utmost importance. Morning vomiting may be given as an example. One is more apt to be misled in a child who has been ill from three to six months than in a child who presents an emergency. Of these cases, 94.7 per cent give a history of over two weeks' duration.

Persistent Periodic Vomiting (Chart 3).—In general it seems that vomiting which is of central origin, whether it be from a brain tumor, meningitis, or craniocerebral injury, is sudden and not preceded by any period of nausea. This has been called, sometimes erroneously, projectile vomiting. Some of the cases presenting difficulty in diagnosis were of children who were considered to have gastrointestinal

disturbances. In most instances careful studies were made of the gastrointestinal system before intracranial tumor was considered. It would seem the part of wisdom that all patients being treated for regulation of diet should have ophthalmoscopic examinations if vomiting persists over one week. This is illustrated by our series, in which 73.6 per cent presented the complaint of persistent periodic vomiting, while 21 per cent complained only of morning vomiting.

An attempt was made to analyze the symptom of vomiting. This was done for two reasons. In the first place vomiting, while not always associated with serious consequences, is a very common complaint of childhood, and in the second place, it was the outstanding symptom in this group. Two types of vomiting were encountered. The first was persistent periodic vomiting which failed to be explained by the physical examination. It occurred at any time during the day but seldom, if ever, awoke a child from his sleep. This is in contradistinction to vomiting due to appendicitis, intussusception and other gastrointestinal disorders in which the child may be awakened with vomiting. If the mother says the child is awakened by vomiting, it usually signifies some intestinal disorder. The second type occurred only in the morning and will be discussed later.

Anyone who observes large groups of children in hospitals must be impressed by the fact that it is a rare thing for a child, regardless of his social status or home training, to vomit without making some attempt to reach for a basin or show other instinctive methods to protect himself and his surroundings. On the other hand, the child with a brain tumor has little or no warning. One may find him with the bedclothing soiled, or, if vomiting is projectile in type, the vomitus may be on the floor or wall. Usually the child is as surprised as the attendant who discovers him.

Headache (Chart 3).—Pediatricians generally agree that it is relatively infrequent for a child to complain voluntarily of headache. If a child complains of headache, a pediatrician should carefully inquire into the cause. At the same time one must learn to differentiate between the headaches described by nervous, interested parents and the headache that a child will mention of his own volition. All will agree that headache in a child is a serious complaint if it is frequent or persistent. The type of headache does not necessarily indicate the location of the tumor. However, it is well known that occipital or suboccipital pain is more common in posterior fossa lesions. This may be associated with stiffness of the neck or suboccipital tenderness. The fact that cerebellar tumors sooner or later will cause a block of the aqueduct of Sylvius with resultant hydrocephalus would indicate that in time the headache may become general. Pain in the forehead, temples, or vertex may occur with a tumor in almost any location. Suboccipital tenderness, however, should be emphasized in view of the

fact that approximately two-thirds of the brain tumors in childhood are below the tentorium. The headache may, or may not, be associated with vomiting. In this series headache was complained of in 63.1 per cent of the cases.

If a child is old enough to answer questions, there is little difficulty in getting the history of headache. He may greet you with the words, "Don't touch my head," even before the question is asked. Younger children will put their hands to their heads or rub their heads on the pillow. When headache is pronounced, the child is usually lethargic and may become comatose.

In adults bradycardia is often associated with headache when intracranial tumors are present. This is usually not the case in children. It was not found in our series.

Disturbance of Gait (Chart 3).—Most of the disturbances of gait have been in the nature of ataxia. Stumbling and falling, especially in younger children, have been prominent. On the other hand, staggering is infrequent in children with *early* fourth ventricle tumors. For a considerable period of time they may be even agile on their feet, being able to climb trees, roller skate, or run like their playmates. Occasionally incoordination was first noticed when the child could not ride his bicycle or use roller skates properly. As the tumor grows and begins to impinge upon or invade the cerebellar hemispheres, gait disturbances become more evident. On the other hand, a tumor beginning in one cerebellar lobe may evidence itself by early gait disturbance. In our series 55.2 per cent complained of gait disturbance. Practically all of these patients had posterior fossa lesions of one type or another. Not all of the cerebellar patients, especially with the fourth ventricle tumors, had ataxia. Loss of balance sense and stumbling in a child is often looked upon as awkwardness by the parents, and little significance is attached to it. It is difficult, often impossible, in a child of two or three years to get valuable information from the gait. It is well known that these children have their good days and their bad days. On one day the examiner may elicit no disturbances in gait; on another the ataxia is only too evident. The mother often calls this to the physician's attention. Incoordination of the upper extremities, while less frequent than of the lower, may occur. The child may be awkward in feeding or dressing himself. He cannot perform fine movements with his hands.

If the tumor is in the vermis, there is usually incoordination of the trunkal muscles. Such a child, if pushed backward from the standing position, cannot save himself from falling by shifting his center of gravity. He falls like a tenpin because he cannot throw his pelvis forward. Again crawling or creeping in young children may be impossible because they cannot synergize the action of their trunkal muscles with those of their extremities.

Hemiplegic gaits may be seen if the lesion is near either motor strip, but these are less frequent in children than in adults.

Convulsions (Chart 3).—Convulsions during childhood are, generally speaking, rather frequent. They may at times be the first clinical manifestation of almost any acute infection. In general it may be said convulsions are most frequently associated with febrile states. One valuable aid in the diagnosis of convulsions due to brain tumor is that they are not associated with any marked elevation of temperature. While epilepsy is not uncommon in children, it was rather striking that not once was this diagnosis made in this series of brain tumors. The characteristics of the typical epileptic fit are well known. The type of convulsion associated with decerebrate rigidity is not infrequent in cerebellar tumors or those about the brain stem but is practically never seen in the true epileptic.

While convulsions do not constitute a very prominent symptom in this series, 31.5 per cent, their presence was almost always of serious import. Convulsions were more frequent in children under two years of age than in the older ones. They were seldom of any localizing value. No instance of jacksonian epilepsy was recorded in this series. In only one instance did a child with a brain tumor survive more than three weeks after the onset of convulsions. This was the case of a five-and-one-half-year-old girl presumably with a fourth ventricle tumor who died three months after admission. Children with tumors who have convulsions are perhaps less likely to have associated loss of sphincter control than epileptics.

Nystagmus (Chart 3).—Nystagmus was present in approximately half of the cases of cerebellar tumor. It was not constant, often coming on relatively late. It should be emphasized that nystagmus is seldom present early in fourth ventricle or even in vermis tumors. About half of the cerebellar tumors were in the midline and consequently did not cause nystagmus. When present, however, especially if associated with headache or vomiting, nystagmus should be considered as very significant. Nystagmus was found in this series in the same proportion as convulsions, namely, 31.5 per cent. The two, however, had no relationship. No attempt will be made to analyze the various forms of spontaneous nystagmus. Suffice it to say that horizontal nystagmus is by far the most frequent.

Morning Vomiting (Chart 3).—In a relatively large percentage of early fourth ventricle tumors morning vomiting may be the only presenting symptom. This may continue for weeks or months before other symptoms appear. Any child with persistent repeated morning vomiting should be looked upon with suspicion from the standpoint of a possible fourth ventricle tumor. Not infrequently these children have been considered as presenting behavior problems or of being of a neuropathic constitution. The vomiting may have been considered

as a subterfuge on the part of the child to prevent him from going to school or from being obliged to perform some other distasteful duty. It is a significant fact that morning vomiting may appear alone for a long time, the child not vomiting at any other time in the twenty-four hours.

In observing these cases we were impressed with the fact that not infrequently a child was sent into the hospital for vomiting but while in the hospital the patient did not vomit. This would seem to be misleading. In an analysis of this, it would seem that we did not bear in mind the difference in routine between the hospital and the home, the main point being that while a child is in the hospital, he is not allowed to be up and about. One is therefore led to believe that morning vomiting may be induced by sudden change of posture associated with arising in the morning. Consequently, these hospitalized children, being kept in bed, are less likely to vomit.

It has been said that a child with morning vomiting, enlargement of the head, and headache gives presumptive evidence of a fourth ventricle tumor.

Ocular Motor Palsies (Chart 3).—Strabismus of one sort or another is relatively frequent among otherwise healthy children. One can always find cross-eyed children in a hospital. Not infrequently operations are performed in children's hospitals for imbalance of ocular muscles. However, there may be a significant neurologic background for these conditions. In seven of our children, 18.4 per cent of the series, bilateral internal strabismus occurred twice, unilateral ptosis and bilateral ptosis once each, and unilateral internal strabismus three times. It is well known that paralysis of the abducens nerve is a notoriously unreliable sign. It is frequently seen in internal hydrocephalus from any cause, the sixth nerve being the longest and consequently most liable to trauma.

Failing Vision (Charts 3 and 4).—A special graph has been made showing the relative frequency of choked discs as compared with the infrequent subjective complaint of failing vision (Chart 4). In only 18 per cent of the cases were visual disturbances mentioned in the history, while ophthalmoscopic examination revealed the presence of choked discs in 73.6 per cent of the series. In several instances the diagnosis of tumor was either missed, or considerably delayed, because the eyegrounds were not examined. In view of the fact that the discs are choked in 73 per cent or more of cases of brain tumor, one cannot refrain from emphasizing again the importance of this examination. Every pediatrician should be able to recognize whether or not the eyegrounds are normal. Ordinary choking of the discs is a characteristic picture and should occasion little difficulty of recognition. One should not wait, especially in children, for a history of failing vision before

examination of the fundi. A child should never be fitted for glasses without first having an ophthalmoscopic examination.

Nausea (Chart 3).—Nausea is difficult to define. It is purely a subjective symptom. It not only implies being "sick to the stomach" but a loathing for food. Patients who are nauseated will not eat. This holds true in children as in adults. When present it occurred relatively late and comprised only 15.7 per cent of the cases. It was not nearly as frequent as vomiting (73.6 per cent). The child with a brain tumor may vomit frequently but in the interim will usually take food readily. We know of no other condition in which this is true except perhaps in pyloric stenosis. In this respect only, do these two conditions resemble one another.

Spinal Fluid Findings (Chart 5).—Spinal fluid examinations were made in 70.2 per cent of the cases. It is generally considered that lum-

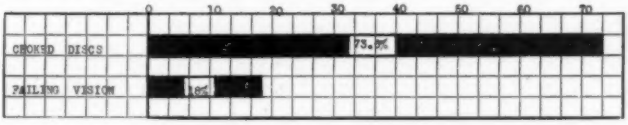

Chart 4.—Graph showing relative frequency of choked discs as contrasted to the infrequent complaint of failing vision.

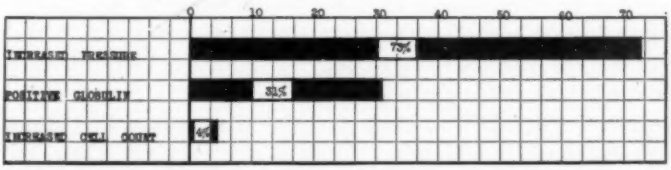

Chart 5.—Graph showing spinal fluid findings in 70.2 per cent of the cases.

bar puncture is attended with considerable risk in cases of brain tumor. This is especially so if a tumor is suspected in the posterior fossa. The danger lies in the risk of herniation of the cerebellar tonsils into the foramen magnum with consequent embarrassment of the medullary centers. In view of the fact that a large percentage of the tumors were in the cerebellar region, we admit freely that a considerable hazard was entailed in carrying out these studies. Fortunately no harmful results occurred.

In spite of the fact that no ill effects followed lumbar puncture, we do not wish to leave the impression that we advocate its promiscuous use. When it is employed, it should be performed carefully in the horizontal position with the use of a manometer. In this way the outflow of fluid can be kept under control and the pressure more accurately measured. The measurement of spinal fluid pressure is one of the most accurate indices of the existing degree of intracranial

pressure and in this respect is of value. Struggling, which frequently occurs in children, during lumbar puncture must be taken into account in estimating pressure readings.

Seventy-three per cent of our spinal fluid examinations showed increased pressure. The pressure, unfortunately, was not accurately measured with a manometer and depended upon the estimation of the observer. In 31 per cent the globulin was increased. This was seldom the case if the tumor chanced to lie in the fourth ventricle. This was contrary to our expectations. The cell count was increased in only 4 per cent of the cases. In this hospital a cell count up to ten is considered within normal limits. In only three cases did the count rise above this, being respectively, nineteen, thirty-three, and one hundred twenty cells. In the three cases of tuberculoma, the first had no spinal fluid examination; the second contained seven cells and no increase in globulin; and the third resulted in a bloody tap and was not repeated.

Errors in Diagnosis (Table IV).—Errors in diagnosis are excusable at some stage in almost every disease. Symptoms are kaleidoscopic; they seldom follow the definite chronologic sequence as described in textbooks. The impression gained at the first examination is often changed after further study. Consequently, there is frequently a wide divergence of opinion between the admitting diagnosis and the final diagnosis in any group of cases. In the series under consideration a correct clinical diagnosis was arrived at in 70.9 per cent of the cases. With a relatively large group of unverified tumors one cannot be sure regarding the series as a whole. Table IV, "Errors in Diagnosis," has been prepared to bring out the differences between the admitting diagnosis and the final diagnosis. The principal source of error in each instance has been listed. In the eleven cases cited the constant source of error which existed was failure to examine the eyegrounds. When this was done, the physician was put on the right track. It demonstrates very clearly the fact that mistakes often happen not because of lack of general knowledge but because of incomplete examination. Three cases tentatively diagnosed as encephalitis have been cited. These all proved at autopsy to be tumors of some part of the cerebellum. The existence of encephalitis, especially soon after the influenza epidemic of 1918, was very frequent. During the latter years it has been seen with diminishing frequency. Postinfluenzal and possibly postvaccinal encephalitis are among the most common forms in children. The encephalitis form of poliomyelitis should always be borne in mind. These conditions are usually associated with a rise in temperature and often with signs of meningeal irritation. Such would not be the case in a tumor. Choking of the discs, while rare, may be present in acute encephalitis.

Dietary disturbances are very common among young children. It is, therefore, not surprising that a case of brain tumor with vomiting should be admitted under this heading. The same may be said of acidosis. Two cases have been listed as behavior problems or neuropathic constitution. Morning vomiting was a presenting symptom in both. They had been followed a number of months in a child's guidance clinic, where it was considered that vomiting was a subterfuge on the part of the child to prevent his going to school. They were treated for some time as behavior problems. Finally fundus examinations, made because of headaches, clarified the diagnosis. One case of

TABLE IV

ERROR IN DIAGNOSIS

ADMITTING DIAGNOSIS	FINAL DIAGNOSIS	SOURCE OF ERRORS
Encephalitis	Tumor, left cerebellum	Eyegrounds not examined.
Encephalitis	Tumor, third ventricle	Eyegrounds not examined. Misinterpretation of history.
Encephalitis	Tumor, right cerebral hemisphere	Eyegrounds not examined. No x-ray study.
Diet regulation	Tumor, third ventricle	Eyegrounds not examined.
Diet regulation	Glioma	Eyegrounds not examined. No x-ray study. No spinal fluid study.
Diet regulation; Acidosis; Allergy	Tumor, fourth ventricle	Eyegrounds not examined.
Acidosis; Sinusitis	Tumor, midline cerebellar	Fitted for glasses without fundus examination.
Behavior problem	Tumor, cerebellum	Eyegrounds not examined.
Rickets	Tumor, left cerebellum	Eyegrounds not examined. Misinterpretation of history.
Swollen arm; Convulsions	Tuberculoma, cerebellum	Eyegrounds not examined. No x-ray study. Spinal fluid not properly examined.
Neuropathic constitution	Tumor, fourth ventricle	Eyegrounds not examined. No x-ray study.

rickets which resulted in death from a tumor of the left cerebellum was incorrectly diagnosed because of lack of eyeground examination and misinterpretation of the history. In reviewing the history in the light of postmortem findings, we find one should have been at least suspicious of a brain tumor. The diagnosis of rickets was correct but had nothing to do with the cause of death; autopsy showed an unsuspected tumor.

One child was admitted with swelling of the arm and draining cervical adenitis. Both were tuberculous. While under treatment he had a convulsion, which was disregarded, and the child was discharged. Upon readmission tuberculous meningitis was suspected, and a spinal fluid examination was made. A bloody tap resulted and the usual tests could not be made. It was not repeated as should

have been done. No roentgen ray study of the skull was carried out. The fundi were never examined. Autopsy revealed a tuberculoma of the cerebellum.

ROENTGENOLOGIC STUDIES

Stereoscopic roentgenologic examinations of the skull are highly important in any case of suspected brain tumor. It is realized that in young children this is difficult, and sometimes impossible, to accomplish. However, the effort should be made. In the majority of cases the findings will consist of increased convolutional pressure atrophy and separation of the sutures. In this series these changes were present in 52.7 per cent of the cases. Convolutional markings alone are perhaps of no great significance, for it has been shown by Eaton[4] that they occur frequently in normal children under the age of twelve. He thinks general nutritional changes may be a factor in their production. When found in conjunction with separation of the sutures, convolutional atrophy has definite significance. This is especially true if accompanied by measurable enlargement of the head. The tendency for the infant to decompress himself by widening of the sutures and fontanels must be kept in mind. When this occurs, signs of increased pressure as manifested by headaches and choking of the discs may be delayed. In certain cases of pituitary disorder alteration in the sella turcica may be present. This would constitute a very small proportion.

Since the use of air as a diagnostic measure was introduced by Dandy[5] ventriculography has been employed with increasing frequency. It is a valuable asset. We have seldom used air when a cerebellar lesion is suspected: first, because internal hydrocephalus, which accompanies these tumors, can be easily recognized in children from ordinary roentgenographic studies and accurately confirmed by Macewen's sign (cracked-pot note elicited by percussion of the calvarium); second, there is considerable risk following ventriculography in obstructive hydrocephalus, a high temperature reaction often resulting unless the air is immediately removed; and third, ventricular estimation can be easily done by simply tapping the ventricles preparatory to a cerebellar exploration. In supratentorial lesions ventriculography has greater value. Encephalography, the introduction of air by spinal route, should probably seldom, if ever, be used in cases of suspected brain tumor accompanied by clinical signs of increased intracranial pressure.

Cysts in the region of the sella turcica may be shown by roentgenologic examination. A case in point will be discussed.

J. R., male, aged nine years, was admitted on June 20, 1928, and dismissed July 15, 1928. He was seen by a number of men on the staff, including one of the writers. Several men felt that he had a brain tumor, probably in the cerebellar region. Vestibular studies pointed to a lesion of the right cerebellopontile angle. A visual field examination, even roughly made, was not recorded. Roent-

genologic studies were conducted, flat plates being used. These consisted of roentgenographs of the head, long bones, chest, and sinuses. No adventitious shadows were seen in the head. This child was taken to the Mayo Clinic where on Aug. 6, 1928, we learned[6] that bitemporal hemianopsia was demonstrated and "a calcification above the sella turcica was revealed by x-ray examination." He was considered to have a cyst near the optic chiasm. At operation it proved to be a calcareocholesteatoma containing a large amount of fluid rich in cholesterol crystals. He was discharged from that institution as improved. It is well pointed out by Bailey[7] that certain tumors about the pituitary region give symptoms simulating cerebellar disease. However, our error in diagnosis lay in the fact that visual field examinations were not made, and sufficiently careful roentgenologic studies were not conducted. Had we found the bitemporal hemianopsia and the suprasellar shadow, both of which were undoubtedly present, the case would have been clarified.

A second case (26-294, Feb. 15, 1926; 26-758, May 31, 1926; and 28-958, May 14, 1928) is called to attention. This case, that of a little girl, nine and a half years old, who had fairly typical signs of hypopituitary disease presenting a picture of Fröhlich's syndrome, first came under observation in February, 1926. Roentgen ray studies of her head showed marked convolutional impressions, some enlargement of the sella turcica, and narrowing of the posterior clinoid processes. A supposed pituitary adenoma was diagnosed, and the child was operated upon. Fragments of what appeared to be a somewhat enlarged pituitary gland were removed. Microscopic sections showed these to be made up of squamous epithelium. The significance of this was not apparent at the time. There was gratifying improvement which lasted for a period of years. Finally her symptoms of headache and visual disturbance recurred, and she was reoperated upon Apr. 19, 1933, when a very large suprasellar, or Rathke's pouch, cyst was encountered. During the intervening eight years, she had developed suprasellar shadows which were plainly seen in subsequent plates and which in themselves were enough to make a diagnosis. She died on Dec. 23, 1933, almost eight years after first being seen; this is the longest survival period of any case. During our period of observation we were permitted to see the laying down of calcium in this craniopharyngeal pouch cyst as evidenced by repeated roentgen ray examinations.

NEUROOTOLOGIC STUDIES (TABLE V)

Neurootologic studies have been of great value. Examination of the eighth cranial nerve in some respects is analogous to the examination of the second and frequently assumes priority over the optic nerve in disclosing the location of an intracranial lesion. Whether or not true choking of the eighth nerve exists in brain tumor cases is a question. However, abnormalities in the function of both auditory and vestibular components of this nerve may be of distinct value. This is particularly true of the intracranial vestibular pathways. The examination of these pathways in children is more difficult than in adults, owing to the children's inability to cooperate. However, certain rather definite conclusions may be drawn in the majority of cases. Differential diagnosis between a subtentorial or a supratentorial lesion can be made with considerable certainty. This in itself is of great value, especially if the lesion be subtentorial, as the usual cerebellar exploration gives adequate exposure to handle any lesion which may be encountered in the posterior fossa.

In thirteen cases neurootologic studies were carried out (Table V). In nine instances in which the diagnosis of a posterior fossa lesion was suggested by means of studies of the vestibular mechanism, eight were correct. In one of these a lesion was predicated in the right cerebellopontile angle. This proved to be a cholesteatoma in the region of the chiasm invading the third ventricle. In another instance the vestibular reactions were considered as normal, but a craniopharyngeal pouch cyst was found at operation. In still another instance,

TABLE V

ANALYSIS OF NEUROOTOLOGIC IMPRESSIONS COMPARED WITH TUMOR LOCATION

NEUROOTOLOGIC IMPRESSIONS	LOCATION OF TUMOR	TYPE OF TUMOR
Postfossa lesion—probably brain stem	Fourth ventricle	Spongioblastoma multiforme
Right cerebellar lesion—pressure on brain stem	Right cerebellar tumor extending into cerebellopontine angle	Glioma (type not given)
Suggest lesion—fourth ventricle	Fourth ventricle tumor	Medulloblastoma (?)
Suggest cerebellar involvement	Left cerebellar lobe	Medulloblastoma
Suggest posterior fossa lesion—not definite	Fourth ventricle—extending to left cerebellar lobe	Medulloblastoma
Suggest posterior fossa lesion—probably brain stem involved. (A frontal lobe tumor will sometimes simulate this.)	Fourth ventricle tumor	Medulloblastoma
Suggest left cerebellar lesion	Cystic tumor from vermis involving left cerebellar lobe	Medulloblastoma
Probably posterior fossa lesion	Vermis—cerebellum	Medulloblastoma
Cerebellopontine angle (left), or cerebellar tumor (left) extending into the angle	Postchiasmal and third ventricle	Cholesteatoma
Picture suggests posterior fossa lesion, probably left cerebellar	Medulla	Spongioblastoma multiforme
Posterior fossa intact	Suprasellar	Rathke's pouch cyst
Intracranial tumor—coma prevents localization	Right temporal lobe	Spongioblastoma multiforme (?)
Midline supratentorial lesion	Right occipital lobe	Spongioblastoma multiforme

in an already comatose child, the tests could not be completed, and no conclusions could be drawn. At autopsy a fourth ventricle tumor was found. Following one neurootologic study a middle supratentorial lesion was predicated. At autopsy a spongioblastoma multiforme of the right occipital lobe was found. Perimetric fields and ventriculography would have made the location of the lesion more precise.

PATHOLOGY (TABLE VI)

End-results in verified brain tumor cases are seldom tabulated or published. Van Wagenen[8] recently has summarized the end-results of 149 cases of verified brain tumors from Cushing's clinic eight years

after operation. The expectancy of the children with gliomas, taken as a whole, was 38.8 mo. The survival period of children with midline cerebellar medulloblastomas was 14.5 mo. The patients with cere-

TABLE VI

TYPE AND LOCATION OF PROVED LESIONS WITH SURVIVAL PERIODS

SEX	AGE	OPERATION	TYPE OF LESION	LOCATION OF LESION	SURVIVAL PERIOD
Female	3 yr. 6 mo.	None	Medulloblastoma	Left cerebellar lobe	4 yr. 6 mo.
Female	2 yr.	Partial removal	Medulloblastoma	Left cerebellar lobe	5 mo.
Female	10 mo.	None	Multiple gliomas	Right and left cerebral hemispheres	1 mo.
Female	11 mo.	None	Medulloblastoma	Fourth ventricle, growing forward	16 days
Female	6 yr.	Exposed—not removed	Medulloblastoma	Fourth ventricle	3 yr.
Male	9 yr.	Exposed by Adson. Partial removal	Cholesteatoma	Postchiasmal and third ventricle	5 yr.+ (may be living)
Male	6 yr.	Partially removed	Medulloblastoma	Vermis—cerebellum	10 mo.
Male	11 yr. 6 mo.	Not removed	Spongioblastoma multiforme	Right occipital lobe	4 yr.
Female	3 yr.	Partially removed	Medulloblastoma	Fourth ventricle	1 yr. (?)
Male	8 yr.	None	Glioma (spongioblastoma multiforme?)	Right temporal lobe	8 mo.
Male	5 yr. 9 mo.	Fragment removed	Spongioblastoma multiforme	Medulla	3 wk.
Male	2 yr. 8 mo.	Partially removed	Medulloblastoma	Left cerebellar lobe	9 mo.
Female	9 yr. 6 mo.	Partial removal on two occasions	Rathke's pouch cyst	Suprasellar	8 yr. 6 mo.
Male	9 yr.	Partially removed	Spongioblastoma multiforme	Fourth ventricle	6 mo.
Female	2 yr.	None	Cystic (colloid ?)	Third ventricle	4 mo.
Male	4 yr.	None	Medulloblastoma	Fourth ventricle, growing forward	13 mo.
Male	7 yr.	Partial removal	Medulloblastoma	Fourth ventricle	Living, over 7 yr.
Female	8 yr.	Ventricle tap	Glioma (unclassified)	Right cerebellar lobe	4 yr.
Female	2 yr.	None	Tuberculoma	Multiple (1) left temporal lobe; (2) right cerebellar lobe; (3) left cerebellar lobe	3 mo.
Male	7 yr. 6 mo.	Partial removal	Tuberculoma; tuberculous meningitis	Right cerebellar lobe	2 yr.
Female	2 yr. 11 mo.	None	Tuberculoma; tuberculous meningitis	Right parietal lobe	10½ mo.

bellar astrocytomas, however, did much better, the average survival period being nine years.

Our group of children in whom lesions were verified showed an unusually high percentage of malignant tumors. The operative results

were discouraging. Indeed, only one child of this entire group is known to be living today. The pathologic records in the earlier cases were incomplete. Twenty-one cases in which the pathology was definite have been listed. There were nine medulloblastomas, five of which originated in the fourth ventricle, one in the vermis, two in the left cerebellar lobe, and one in the right cerebellar lobe. The longest survival period for these tumors was over seven years, in a lad who has had intensive postoperative high voltage therapy. The shortest survival period of this group was sixteen days, in an eleven-month-old infant. There were two cases of spongioblastoma multiforme, one occurring in the right occipital lobe and the second, an atypical form of this tumor, invading the medulla. The first was explored, but the tumor was not removed at operation. The child lived four months. A third (probably a spongioblastoma multiforme) occurred in the right temporal lobe. These tumors were all supratentorial as compared with the subtentorial medulloblastomas mentioned above. There were two unclassified gliomas, the second of which was multiple occurring in a ten-month-old infant. No cystic tumors were encountered, and no astrocytomas were identified. There was one cystic tumor of the third ventricle in a two-year-old child. This case occurred early in the series, and the specimen has been lost. One wonders if it may not have been the relatively benign colloid type of cyst occurring in the third ventricle, which has recently been so well described by Dandy.[9] A second unusual congenital tumor was a cholesteatoma in the region of the postchiasm and third ventricle. There was one typical Rathke's pouch cyst with a survival period of eight and one-half years from the earliest symptom. During this little girl's life the tumor was twice operated upon and partially removed. Suprasellar calcification was seen to develop during this interval. There were three tuberculomas, one partially removed from the right cerebellar lobe and a second in the right parietal lobe, which was not explored, and a third presenting multiple tuberculomas in the left temporal, right cerebral, and left cerebral lobes, respectively. All of these children died of tuberculous meningitis. The longest survival period was two years; the shortest survival period three months.

SUMMARY AND CONCLUSIONS

A résumé of thirty-eight cases of verified and highly probable intracranial tumors in children has been attempted. None of the children had reached his thirteenth birthday, and the majority of them were under ten years of age. The group as a whole was younger than is usual in preadolescents, in whom the age of puberty is approaching. More exact diagnoses should have been made and better results obtained. However, the same could probably be said in the majority of

children's hospitals in this country so far as the diagnosis and treatment of such lesions is concerned.

Much more could be accomplished by greater attention to the common presenting symptoms, i.e., persistent periodic vomiting, headache, disturbance in gait, ocular motor palsies of various types, enlargement of the head, failing vision, nausea, convulsions, morning vomiting, and nystagmus. These are of common occurrence. They have been recorded in the relative frequency of their appearance.

Doubtless many cases of cerebral tumor in small children are not recognized. Histories should be more carefully taken. One can learn much from mothers. The pitfalls in diagnosis, as we have found them in reviewing our cases, have been pointed out. Without exception the lack of use of the ophthalmoscope has been most evident. We have seen children treated as behavior problems because they vomited their breakfasts—children in whom brain tumors were later diagnosed. In other children extensive gastrointestinal investigations, which could have been obviated by the use of the ophthalmoscope, were carried out because of vomiting. We have seen children with failing vision from brain tumors fitted to glasses without fundus examination. We believe that if every pediatrician would use his ophthalmoscope diligently many cases, otherwise overlooked, would be correctly diagnosed. Little that is new has been presented in this report. We trust, however, that the more important symptoms have been sufficiently emphasized to aid in earlier diagnoses of brain tumor in children.

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SUPPURATION OF THE MIDDLE EAR COMPLICATED BY LABYRINTHITIS, SINUS THROMBOSIS, CEREBELLAR ABSCESS, AND CEREBELLAR HERNIA WITH COMPLETE RECOVERY

CASE REPORT

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SUPPURATION of the middle ear complicated by labyrinthitis and sinus thrombosis is so infrequently seen as to warrant its report. However, the addition of a disturbing complicating factor of a cerebellar abscess with a herniation of the brain through the original mastoid incision certainly increases the interest and rarity of such a development. A case such as this with complete recovery except for the brain protrusion at the site of the original operation is reported.

A short discussion of the pathway of invasion of the infection to the labyrinth and its spread to the lateral sinus and cerebellum will follow. To quote F. W. Watkin-Thomas,[1] "the path of invasion is usually (1) through the bone by invasion; (2) through the windows either by necrosis or loosening of the stapes or destruction of the membrana tympani secundaria of the round window (this is the more common route in the acute cases); (3) through perilabyrinthine cells (rare); (4) erosion of superior canal by extradural abscess (rare); and (5) operative injury to external canal of dislocation of the stapes."

After the labyrinth became involved in our case, the infection spread rapidly to the sigmoid sinus. J. G. Druss[2] said, "Infection of the labyrinth may spread to the sigmoid sinus along preformed as well as along newly formed pathways. The saccus endolymphaticus and the labyrinthine veins are the most common of the preformed routes. The newly formed routes consist of fistulas from within the labyrinth through the semicircular canals or through the body of the labyrinth. The saccus endolymphaticus is a narrow pouch between the layers of the dura, which communicates with the endolymph space of the labyrinth through the ductus endolymphaticus. It is situated in the posterior surface of the petrous pyramid, midway between the medial border of the sigmoid sinus and the internal auditory meatus. An infection in the saccus may spread between the layers of the dura and produce a cerebellar abscess; it may involve adjacent bone and produce a huge extradural abscess; it may involve the pia arachnoid and cause meningitis or finally it may extend along the dura to the sinus and cause sinus thrombosis. Infection

of the labyrinth may reach the sigmoid sinus through the labyrinthine veins which empty into the inferior petrosal veins or the jugular bulb. From these structures an infection may spread laterally to the sinus."

CASE REPORT

A girl, six years old, was admitted to the hospital on June 6, 1931, complaining of pain, fever, and discharging right ear following an upper respiratory infection. The family history is unimportant. The child complained of an earache thirteen days before admission. There was a spontaneous rupture of the right drum followed by a profuse purulent discharge in twenty-four hours. The physical examination of the child was essentially negative except for the local ear findings. There was a profuse purulent discharge from the right ear canal with definite tenderness over the mastoid tip. There was no swelling in the postauricular region. Otoscopic examination revealed that the discharge was pulsating. There was a small perforation in the drum. A definite sagging of the posterior wall in the bony meatus was observed. Blood study at this time showed W.B.C., 19,600; polymorphonuclears, 87;

Fig. 1.

lymphocytes, 13 per cent. The temperature was 103° F. The progress of the case can be followed more closely by a study of the continuation notes of the hospital record.

"June 5, 1931, P.M. A right mastoidectomy was performed in the usual manner. At operation the mastoid cells were filled with greenish pus; the body and antrum showed considerable softening. The sinus was uncovered at the knee and was normal in appearance.

"June 8, 1931. Three days postoperative. The child complained of marked dizziness on attempting to sit up. There was definite nystagmus to the left (first degree). Hearing was definitely involved on the right side (noise test). There were no signs of meningeal irritation or involvement. The impression at this time was serous labyrinthitis (complete final recovery without loss of hearing proved this diagnosis). Temperature still ranging between 103° and 104° F.

"June 11, 1931. Child was desperately sick. Temperature rose to 106° F. Blood culture positive for *Streptococcus hemolyticus* (20 colonies in 1 c.c.). Blood study at this time revealed hemoglobin, 60 per cent; red cells, 3,400,000; white cells, 32,700; polymorphonuclears, 81 per cent; lymphocytes, 19 per cent. Ligation of right jugular was immediately performed. Sinus wall was grey and thick. Mural

clot found. Usual operation performed. Transfusion with 200 c.c. of blood given.

"June 12, 1931. No meningeal signs present. Nystagmus to left still present. No petechiae or evidence of any metastatic involvement present.

"June 14, 1931. Temperature was still intermittent. The child was irritable and hyperesthetic. Left lower extremity was extended and resists all motion, especially at knee, where child complains of marked pain on flexion. No swelling, local heat, or joint tenderness made out. Child was probably localizing a purulent focus in left hip. Second transfusion with 175 c.c. blood.

"June 15, 1931. Child was taken to operating room for sinus dressing. Sutures were removed. Swelling of cerebellar tissue in back of sinus was noticed. Dura was incised and large amount of pus obtained. Iodoform gauze was inserted.

"June 18, 1931. Redressed. There was a beginning definite herniation of cerebellum behind sinus into wound.

"June 24, 1931. Marked swelling of left hip, definite tenderness, and fluctuation noted. Incised and drained.

"June 31, 1931. Herniation of cerebellum filling the entire mastoid wound.

"July 5, 1931. Hip healed. Temperature, flat. Mastoid wound was closed except for granulation tissue covering incision with slight pulsating cerebellar hernia behind it (Fig. 1). Child discharged from hospital.

"Aug. 15, 1934. Child fully recovered and well except for herniation."

SUMMARY

1. The pathways of infection from the middle ear to the labyrinth, sinus, and cerebellum are discussed briefly.

2. A case of suppurative middle ear infection with labyrinthitis, sinus thrombosis, and cerebellar abscess with herniation is reported.

3. The presence of a hernia at the site of the mastoid wound is especially noted.

4. Plastic repair of the hernia was considered and after consultation with a neurosurgeon was decided against because of the danger of complicating meningitis.

REFERENCES

1. Watkins-Thomas and Yates: Principles and Practise of Otology, p. 417.
2. Druss, J. G.: Arch. Otolaryng. 19: 671, 1934.

135 EASTERN PARKWAY

AN ANALYSIS OF ONE HUNDRED CASES OF ACUTE POLIOMYELITIS

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DURING the summer and fall of 1932 Philadelphia and the surrounding vicinity experienced an outbreak of acute poliomyelitis of epidemic proportion. From July to November 687 cases were reported to the Department of Public Health; of this number, 100 cases were hospitalized in the Children's Hospital of Philadelphia.

Poliomyelitis in its historical, etiologic, and other aspects has been presented so recently in the monograph by the International Committee for the Study of Infantile Paralysis that we are concerning ourselves in this paper with a statistical analysis only of the data available in this group of cases.

INCIDENCE

1. *Seasonal.*—Chart 1, a graphic representation of the number of cases admitted to the hospital over fifteen-day periods, shows that the maximum point of admission was reached in the last week of August and the first week in September. This peak is in conformity with the curve which Aycock (323)† has charted showing the seasonal distribution of poliomyelitis in the northern United States.

2. *Age.*—The age of the patients in this series varies from six months to twelve years, twelve years being the upper age limit for admission to the Children's Hospital. The age distribution is graphically depicted in Chart 2. It is quite obvious that the bulk of the cases (51 per cent) lies between the ages of eighteen months and five years, with the maximum incidence at four years.

3. *Sex.*—There is a very slight preponderance of males over females, 55 per cent of the patients being male; thus the ratio of male to female patients is 1.22 to 1. Of the 36,000 cases summarized by the International Committee for the Study of Poliomyelitis (407), the ratio was 1.3 to 1.

4. *Color.*—In this series of 100 cases thirty-one were negroes. This percentage of negroes did not seem unusual to us since the Children's Hospital is situated in an area in which there is quite a large negro popu-

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*Work on thesis for master's degree submitted to the Graduate School of Medicine, University of Pennsylvania for postgraduate work.

†Free reference has been made to the *Survey from the International Committee for the Study of Infantile Paralysis*, published by the Williams & Wilkins Company, 1932. The page references throughout this paper are to this volume.

lation and since negroes approximated 40 per cent of our total admissions in 1932. However, Armstrong in a series of 240 cases in Chicago during 1916 found only four negroes with this disease even though there was quite a large negro population in that city. From his figures one might conclude that a racial immunity exists, a conclusion not warranted from our data, nor from the data collected by the Department of Public Health.

5. *Constitutional Factors.*—The state of nutrition of eighty-five patients was definitely described in our records, and, while actual weights were not noted in every case, the nutritional state was found to be good

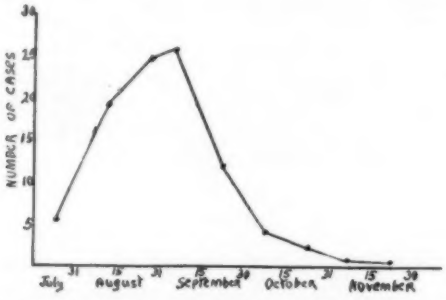

Chart 1.—Seasonal distribution of poliomyelitis.

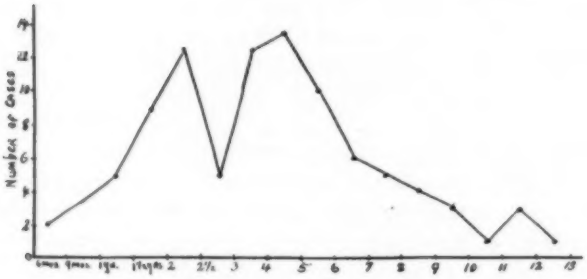

Chart 2.—Age incidence.

in forty-nine cases, fair in twenty-four, and poor in twelve. This is in keeping with the observation of the early writers on poliomyelitis, who stated that it was the healthy, well-developed child who seems most susceptible to the disease.

The diet was specifically noted in eighty-five of one hundred cases. Forty-nine of this number had received a good diet, one which provided ample calories and contained a sufficient amount of protein together with an abundance of green vegetables and vitamins. Twenty-four of the eighty-five children were considered to have had a fair diet, which contained only a moderate supply of green vegetables, vitamins, and protein.

The remaining twelve patients had received a diet which was poor in these essential elements. The nutritional status as tabulated in the preceding paragraph is closely correlated to these dietary differences.

The red blood cell count was studied in seventy-six of the hundred cases. In fifty-six of this number the count was between 4 and 5 millions. In twenty of the cases the red blood cell count was found to be between 3 and 4 millions. The lowest figure was 3,200,000. The percentage of hemoglobin was recorded in seventy-seven cases and ranged between 75 and 100 per cent (Sahli) in fifty-one cases and between 60 and 75 per cent in twenty-one cases.

It would appear from these figures that the disease did not single out the poorly fed, poorly nourished, or anemic child.

6. *Blood Types.*—There have been many conflicting reports concerning the susceptibility of individuals of the various blood groups to poliomyelitis. We have studied the blood types of sixty-seven of our patients. From the results shown in Table I, it would appear that the individuals of no one group were more susceptible to poliomyelitis than those of another.

TABLE I

INCIDENCE OF BLOOD GROUPS IN OUR SERIES OF CASES OF POLIOMYELITIS AND THE NORMAL AVERAGE IN CHILDREN'S HOSPITAL

	I	II	III	IV
Nonpolio cases (per cent)	5	40	10	45
Polio cases (per cent)	3.5	36.7	17.5	42

7. *Family Incidence.*—Our 100 cases represented ninety-two families. One case was recognized clinically in each of eighty-four of these families. Two cases were found in each of six families; on two occasions three cases were discovered in a family. In only eight cases was there a definite record of some other illness in the families of the patients with poliomyelitis. The nature of these illnesses was not known. It is possible that they were abortive poliomyelitis infections and that the incidence of multiple cases in families was much higher than the above figures indicate.

8. *Prophylaxis.*—We shall not discuss at length the value of the various types of prophylaxis against poliomyelitis. However, of the 100 cases studied, four had received citrated whole blood from a parent as a prophylactic measure. One of these four patients received 60 c.c. of whole blood intramuscularly six days before he was discovered to be suffering from poliomyelitis; two received it ten days before the onset of the disease; and in the fourth patient the disease was discovered two weeks after injection. None of these patients developed definite paralysis. It would not seem from these results that we had obtained as

complete a protection from the disease by the administration of adult blood as was found to be the case in the report of the Bradford, Pa., epidemic. It is, however, interesting that none of these four patients developed paralysis, when the incidence of paralysis in our total group was 48 per cent. Possibly the blood obtained from these adults may have had little antiviral potency.

TYPES OF CASES

In the grouping of our cases we used the classification formulated by the New York City Department of Health, which was modified by the International Committee for the Study of Infantile Paralysis (186).

Since in our series neither the abortive nor the ataxic type was recognized, our cases may be grouped into one of three types, viz.:

(1) Nonparalytic Type: This group includes those cases in which no paralysis or muscle weakness was noted, but in which other clinical signs of poliomyelitis were found and spinal fluid changes were observed.

(2) Type With Subcortical Paralysis: This group includes those patients who showed definite paralysis or weakness of the muscles supplied by the spinal or cranial nerves; thus patients in whom there was evidence of bulbar palsy are included in this group.

(3) Encephalitic or Cerebral Type: In this group are placed those cases characterized by cerebral involvement, usually indicated by prolonged stupor, drowsiness, or convulsions.

Some of the cases were rather mixed in type, and these are classified according to their predominating symptoms.

Of our one hundred cases, fifty-two were of the nonparalytic, forty-three of the subcortical, and five of the encephalitic type.

SYMPTOMATOLOGY

It is generally agreed by all writers that the symptomatology of poliomyelitis is highly varied, and this is certainly borne out by an analysis of the present series. Chart 3 represents the incidence of the various constitutional symptoms in the 100 cases studied.

1. *General.*—Fever: In 91 per cent of the cases the temperature was found to be elevated on admission, or a very definite history of fever was obtained. The range of temperature varied considerably although seventy-two of the patients had rectal temperatures between 100° and 102° F. There were six patients in whom the temperature was above 104° F., including one whose temperature reached 107° F. Thirteen patients who gave a definite history of fever before admission were afebrile during their stay in the hospital. Only nine patients were free of fever during the entire illness, as far as we could determine. It is very possible that these children at one time or another did have some fever which escaped notice.

The duration of the fever was also quite variable, as is shown in Chart 4. In the majority of instances the febrile period was from one to four days (fifty-six cases). Sixteen patients remained febrile for a period ranging from five to nine days, while one continued to have fever for eleven days, and one for sixteen days without any complicating cause. It is quite obvious that in our series the characteristic temperature curve is one with a sharp rise at the onset of the disease and an early drop by crisis. In no instance have we encountered a temperature

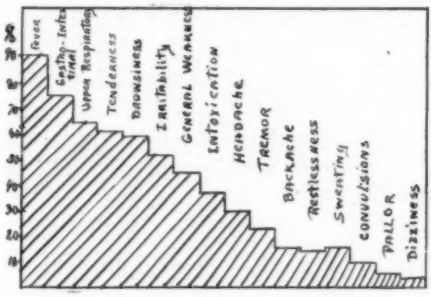

Chart 3.—Relative frequency of symptoms.

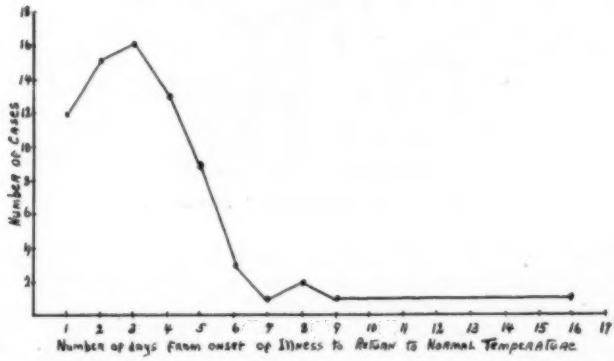

Chart 4.—Number of days from onset of illness to return to normal temperature.

curve described by Draper as the "dromedary" type. All of our febrile patients manifested the type of onset which the International Committee for the Study of Infantile Paralysis found to be the most common, viz.: "By far the most common type of onset . . . is that in which the symptoms of systemic infection progressed rapidly and uninterruptedly to those indicating an involvement of the central nervous system."

Hyperesthesia: Marked tenderness was a striking finding in 63 per cent of our cases. This was elicited sometimes by active motion, sometimes by passive motion, but always by deep pressure. The onset of

hyperesthesia was usually early in the disease. In the nonparalytic type this was rather a transient symptom, while in the paralytic type it was protracted.

Drowsiness: This was also an early symptom found in 59 per cent of the cases. It was present in varied degrees in all three types of cases. Some patients who showed marked drowsiness made complete recoveries, whereas others exhibiting little initial drowsiness suddenly developed bulbar palsy with stupor and died.

Headache and Backache: These symptoms were of relatively low incidence in the total group (Chart 3), but in children over two and one-half years of age, who were hence able to localize their pain, the incidence was greater. In this latter group, headache occurred in 46.6 per cent and backache in 26.6 per cent.

Irritability, weakness, and tremor, were rather frequent. Restlessness and sweating occurred occasionally. Convulsions developed in 10 per cent of the cases.

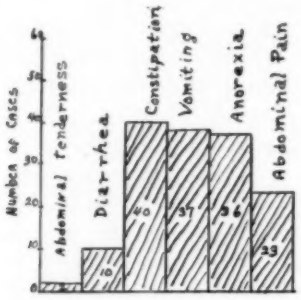

Chart 5.—Gastrointestinal symptoms.

2. *Gastrointestinal.*—Symptoms referable to the gastrointestinal tract were noted in 73 per cent of the cases. As can be seen from Chart 5, constipation, nausea, and vomiting were most common. Anorexia, which occurs so often in all febrile diseases, was also common here. The frequency of abdominal pain was surprisingly high, and because of its severity a number of these patients were very carefully observed for an acute surgical abdominal condition. This pain was often localized in the rectus muscles. At times it was unilateral, and at other times, bilateral. It was accompanied by hyperesthesia in the involved area. Definite rigidity was lacking.

3. *Respiratory.*—Definite symptoms and signs of respiratory infection were noted in 67 per cent of the patients, although a history of sore throats and coryza was obtained in only nine, and a history of cough, in seven. The great frequency of infection in the nasopharynx in poliomyelitis is clearly indicated by the accompanying Chart 6.

Sixteen of the patients showed evidences of respiratory embarrassment. In every case the dyspnea was accounted for either by bulbar paralysis or by paralysis or weakness of the intercostal muscles or diaphragm. When the dyspnea was due to bulbar palsy, it was constant and required the uninterrupted use of the respirator. Dyspnea caused by paralysis of both the diaphragm and intercostal muscles was also constant. In those cases in which either the intercostal muscles or the diaphragm alone were weak or paralyzed, the dyspnea was intermittent and was less severe. Cyanosis accompanied the dyspnea in six of the sixteen patients. None of our patients gave any evidence of cardiac damage attributable to poliomyelitis. Two of the patients were discovered to have systolic murmurs, but without any associated cardiac enlargement. These murmurs were considered to be functional in nature.

4. *Nervous System.*—Chart 7 shows the frequency of such disorders.

While full or bulging fontanel was found in only four cases, these represent 50 per cent of the patients under one year of age. Whenever

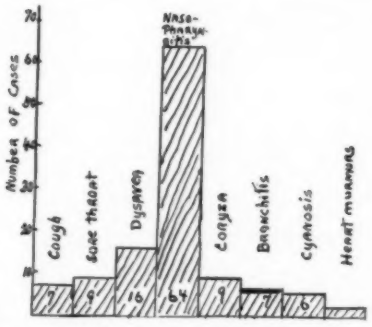

Chart 6.—Cardiorespiratory symptoms.

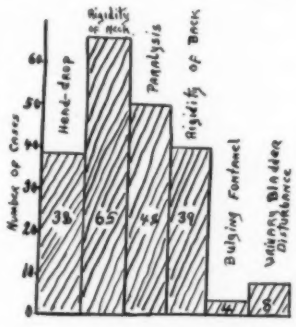

Chart 7.—Nervous symptoms

there was rigidity of the back, there was also true rigidity of the neck. The frequency of a positive Kernig sign was not recorded because in the treatment of our patients serum was injected into the gluteus muscles immediately after admission, making this sign wholly unreliable. Some patients showed trophic disturbance resulting from pressure. Many showed vasomotor imbalance, as evidenced by a tache cérébrale, mottling of the skin, and coldness of the extremities with cyanosis. Catatonia was seen in two cases. With the drowsiness and hyperesthesia, as listed under the general symptoms, the patients often presented most confusing pictures for differential diagnosis. The nervous manifestations frequently resembled those seen in other diseases. For instance, a case of tuberculous meningitis was suspected of being poliomyelitis for several days; and two cases of bacillary dysentery, because of their central nervous system symptoms, were treated as poliomyelitis until the characteristic stools appeared.

TABLE II

DISTRIBUTION OF PARALYSIS

	CASES
Both legs	10
One leg (2 right, 5 left)	7
Both legs and both arms	4
Both legs and one arm	4
One arm (3 right, 4 left)	7
One arm and one leg, same side (right)	2
One arm and one leg, opposite sides	1
Both arms	1
Both arms and 1 leg	0
Girdle	
Abdominal muscles, 11	
Diaphragm and intercostal muscles, 6	17
*Cranial nerves	12

*We have substituted this heading for the one which Lovett calls "Facial Alone." These cranial nerve palsies were distributed among the various nerves as follows:

Oculomotor	5
Facial	5
Oculomotor and Optic (Child appeared not to see; however, ophthalmoscopic examination was negative)	1
Glossopharyngeal	4
Glossopharyngeal, pneumogastric, and facial	1
Glossopharyngeal, pneumogastric, and oculomotor	2

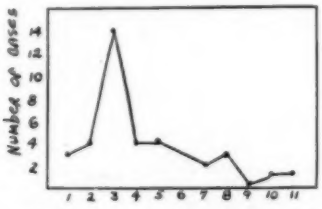

Chart 8.—Relation of onset of paralysis to day of illness.

6. *Genitourinary System.*—The one disorder recorded was retention of urine, which occurred in nine cases, being present only in the acute stage of the disease and clearing spontaneously.

7. *Glandular System.*—No case of cervical or other lymph node enlargement was recorded. In no instance was the spleen noticeably enlarged.

8. *Paralysis.*—Incidence: Of the 100 cases constituting this series, forty-eight developed definite paralysis.

Interval Between Onset and Paralysis: In forty cases we have been able to establish this time interval. The average duration was 4.15 days (Chart 8). In only two patients of this group did paralysis occur on the first day of the disease. The frequently described and dramatic picture of a previously healthy child awaking in the morning with paralysis was not observed in our group. There seemed in each instance to have been some prodromal symptoms. In the majority of our cases, paralysis occurred on the third day of illness. In several instances the paralysis seemed to be of a progressive nature, not reaching its max-

imum for several days. It appeared that as long as an elevation of temperature persisted there was a possibility of the paralysis extending to heretofore uninvolved muscles. We were much impressed by the frequency with which orthopedic examinations detected mild degrees of muscular weakness which had been entirely overlooked during the routine observations.

Distribution of Paralysis: In this presentation we are following the classification of distribution adopted by Lovett.

TABLE III

MUSCLE GROUP PARALYZED

	MUSCLE GROUP	CASES
Shoulder	All	3
	Abductors	22
	Adductors	18
Upper Arm	All	5
	Extensors	10
	Flexors	3
Forearm	All	4
	Extensors	3
	Flexors	2
	Pronators	1
	Supinators	1
Hand	All	4
	Extensors	3
	Flexors	2
	Abductors	2
	Adductors	1
Hip	All	17
	Abductors	14
	Extensors	11
	Adductors	11
	Flexors	5
Thigh	All	17
	Abductors	16
	Extensors	16
	Flexors	5
	Adductors	5
Leg	All	15
	Flexors	14
	Extensors	11
	Abductors	9
	Adductors	6
Foot	All	15
	Flexors	12
	Abductors	9
	Adductors	6
	Extensors	3

In Table III, a summary, we are recording the various muscle groups involved in the paralysis. Our figures are in accord with those of Lovett, who found that one or both legs were the parts most frequently involved. The incidence of cranial nerve involvement in our group (12 per cent) is in striking agreement with that reported in the series of Ruhräh and Mayer (177). While abdominal muscle paralysis occurred in 72 per cent of a series cited by the International Committee (173), only 23 per cent of our paralyzed patients had involvement of the abdominal wall musculature.

Reflexes: In the ninety-three patients on whom we have data, the reflex changes were as follows:

(a) Twenty-six showed no reflex changes at any time during their illness; none of these cases developed any palsy.

(b) Sixty-seven patients exhibited reflex abnormalities, either hyperactivity, hypoactivity, or loss of the reflexes. Of these sixty-seven, nineteen did not develop paralysis. Table IV shows the types and distribution of the reflex abnormalities in these nineteen cases.

TABLE IV

TYPES OF ABNORMAL REFLEXES IN 19 PATIENTS WHO DID NOT DEVELOP PARALYSIS

PATIENT	PATELLAR	ACHILLES'	CREMASTERIC	ABDOMINAL	TRICEPS	BICEPS	PUPILLARY
F. K.	Absent	Absent					
A. Z.	Hyper.	Hyper.		Hyper.	Hyper.	Hyper.	
D. S.	Absent	Absent		Absent			
M. R.	Absent						
J. B.	Absent	Absent	Absent	Absent			
C. S.	Absent	Absent					
J. C.	Hyper.						
R. E.	Hyper.	Absent		Hyper.	Hyper.	Hyper.	
E. S.	Diminished			Absent			
E. S.	Hyper.	Hyper.		Diminished			
W. B.	Absent	Absent		Hyper.			
E. M.	Absent	Absent		Hyper.			
D. G.	Hyper.	Hyper.		Hyper.	Hyper.	Hyper.	
E. M.	Diminished			Absent			
H. M.			Diminished				Sluggish
M. B.	Diminished	Diminished					
J. D.			Absent	Absent			
R. G.				Absent			
D. L.	Absent	Absent					

From these data we conclude that one cannot predict with certainty by the status of the reflexes whether or not a patient will develop paralysis, except in those instances where normal reflexes are present. We were unable to establish the time relationships between the development of abnormal reflexes and the onset of paralysis.

LABORATORY DATA

1. *Spinal Fluid.*—The spinal fluid of ninety-six patients was studied. The first spinal fluid was obtained immediately after admission to the

hospital, and in thirty-nine cases a second, and sometimes a third, examination was made during the course of the disease. In every case the spinal fluid was examined within an hour after the lumbar puncture.

Gross Appearance: The spinal fluid obtained by lumbar puncture was opalescent in eleven cases and clear in eighty-five.

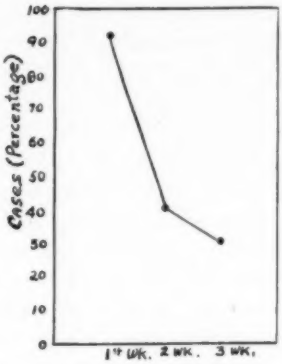

Chart 9.—Percentage of cases showing elevated spinal fluid cell counts with relation to week of illness.

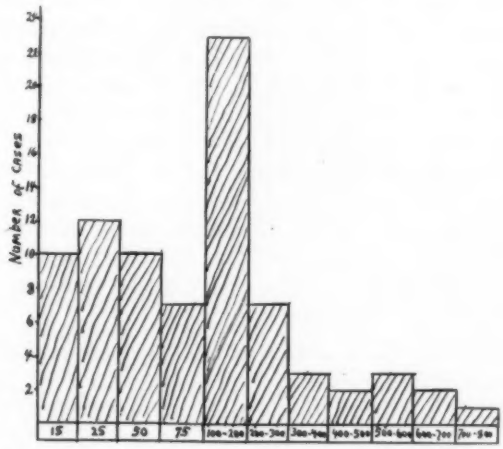

Chart 10.—Spinal fluid white cell counts (per c. mm.).

Cell Count: The spinal fluid cell count made during the first week following onset was found to be elevated in most instances. Of the eighty-two cases studied in this period, only seven did not have a cell count above the normal limits. Our laboratories accept the upper limit of normal to be ten cells per cubic millimeter. One of these seven patients showed an increase on subsequent examination. Other patients in subsequent punctures also showed increases beyond their first counts. Speci-

mens obtained between seven and fifteen days following the beginning of the disease were very much less likely to show pleocytosis. Only ten of twenty-three patients during the second week exhibited an abnormal number of cells in their spinal fluid. When the spinal fluid was studied two or more weeks after onset, only eleven out of thirty-five patients showed an increase in the number of cells. This is graphically shown in Chart 9, which illustrates the tendency of the spinal fluid to return to normal with the subsidence of the active period of the disease. The actual degree of pleocytosis varied widely. However, the majority of our cases had spinal fluid cell counts above 100, as can be seen from Chart 10. The highest figure reported was 740 cells per cubic millimeter. In general the increase in the spinal fluid cell count was due to a rise in the number of lymphocytes. However, in many instances there were also considerable numbers of polymorphonuclear cells found. The polymorphonuclear response was much more frequent in the early days of the disease than in the later stages. It is sometimes said that early in the disease the spinal fluid response is a polymorphonuclear one and that later in the disease the response is lymphocytic. This was found to be true in only 18 per cent of the cases in our series. Twenty per cent of the differential counts made on spinal fluid obtained after three weeks of the illness still showed some polymorphonuclear cells. We are led to the conclusion that the presence of polymorphonuclear cells in the spinal fluid is not associated with any particular period of the disease but that they are found in large numbers only in the early stages. In addition to the lymphocytes and polymorphonuclear cells, endothelial cells were occasionally found in the spinal fluid. Frequently degenerated cells were found in the spinal fluid, even when the examination was performed immediately after the fluid was obtained. It was usually impossible to determine the nature of such cells, and their significance is unknown. The differential counts were usually made on centrifuged specimens stained with methylene blue.

Study of the spinal fluid cell counts seen made it apparent that a high count did not necessarily mean a severe illness. On the contrary, the reverse is suggested from our findings. As can be seen from Chart 11, paralysis occurred less frequently when the cell count was above 300 per cubic millimeter than when it was below this figure. The patients showing evidences of meningeal irritation usually had a high cell count with the polymorphonuclear cell predominating.

There were eighty-six patients with a cell count below 300 in the first fluid obtained. Of these, forty-four (52 per cent) exhibited detectable paralysis. Ten patients had more than 300 cells, and of these patients only two became paralyzed (20 per cent). Despite the fact that this latter group consisted of so few cases, we are inclined to attach importance to these figures.

Globulin: The spinal fluid of eighty-three patients was examined for globulin; the examination was made by adding a few drops of a saturated aqueous solution of ammonium sulphate to the fluid. The globulin was considered to be increased when this test produced a cloudiness, which is proportional to the amount of globulin present. Of these eighty-three spinal fluids, seventy-seven showed an increase in globulin content. The amount of globulin increase did not bear any definite relationship to the number of cells in the spinal fluid. Sometimes the globulin was increased when no cells were found, while in other instances there was only a slightly increased globulin content in the presence of a high cell count. The change in globulin content persisted longer than any of the other abnormalities noted in the spinal fluid;

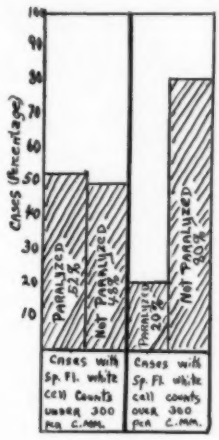

Chart 11.

in many cases an increase in the globulin was present after all other pathologic findings had disappeared.

Sugar: Quantitative sugar estimations were carried out on 104 samples of spinal fluid. Twenty-three per cent of these determinations were found to be elevated above 72 mg. per cent, which was considered to be the highest normal figure. In no case was there any decrease in the spinal fluid sugar. There was no definite relationship between the changes in sugar content and the various other spinal fluid changes.

Chloride Content: This was determined in 100 cases. In only four instances was there any reduction below 650 mg. per cent (as Cl), which was considered the lowest normal value. The spinal fluid of the remaining ninety-six cases showed a chloride content very close to 700 mg. per cent.

Pressure: Spinal fluid pressure readings were reported in most of the cases and showed wide variations. In general a moderate elevation

of pressure was found. However, because of the inaccuracies which are inevitable in the measurement of spinal pressure in children, due to their struggling, little significance can be attached to any detailed analysis of these findings. In no case was the spinal fluid pressure high enough to be considered dangerous per se.

Wassermann Reaction: The spinal fluid Wassermann reaction was carried out in twenty-five cases and was found to be negative in all of them.

Pellicle Formation: A very slight pellicle was formed in nine spinal fluid samples after they were allowed to stand.

2. *Urine.*—Seventeen patients showed a "trace" or "faint trace" of albumin in the urine. Fourteen children who had been vomiting or whose fluid intake had been insufficient were found to have ketonuria. The urine of two children contained granular casts on one or two occasions.

3. *Serology.*—The blood Wassermann reactions of twenty-four of our patients were recorded. Twenty-three were negative; one was positive. Two of the twenty-four patients were attending our clinic for antisyphilitic treatment. The positive Wassermann found was in one of those two children.

4. *Hematologic Findings.*—The hemoglobin and erythrocyte findings have already been discussed. We obtained white blood cell counts in seventy-one cases and differential counts in seventy-nine. These counts were all made on the day of admission and therefore in the acute stage of the disease.

Table V summarizes these findings.

TABLE V

TOTAL WHITE COUNTS

CASES	THOUSANDS
15	From 5 to 7
32	From 7 to 10
28	From 10 to 15
4	Above 15

DIFFERENTIAL WHITE COUNTS

UNDER THREE YEARS OF AGE			OVER THREE YEARS OF AGE		
I. Polynuclears	Normal (45-55%)	18	I. Polynuclears	Normal (55-65%)	20
	Increased (> 55%)	17		Increased (> 65%)	11
	Decreased (< 45%)	5		Decreased (< 55%)	8
II. Lymphocytes	Normal (40-50%)	18	II. Lymphocytes	Normal (35-45%)	17
	Increased (> 50%)	5		Increased (> 45%)	7
	Decreased (< 40%)	17		Decreased (< 35%)	15

MORTALITY

Seven deaths occurred in our 100 cases. A brief summary of these seven cases follows. Three of these patients were under eighteen months

of age. Since there were twelve patients in our entire series under that age, the mortality rate in the patients of this age group was 25 per cent. This high mortality during infancy is in keeping with that reported by other observers (352-353).

TABLE VI

FATAL CASES

	AGE	SEX	RACE	DAYS OF ILLNESS	TYPE OF CASE
D. R.	6 mo.	F	Black	Died on 9th day, four days after admission.	Subcortical first, then encephalitic symptoms developed.
A. P.	9 mo.	M	White	Died on 5th day, day after admission.	Subcortical, also encephalitic symptoms. Never regained consciousness.
L. R.	15 mo.	F	White	Died on 6th day, day after admission.	Subcortical—paralysis of pharyngeal and laryngeal muscles.
E. N.	30 mo.	F	White	Died on 5th day, day of admission.	Subcortical—paralysis of larynx and pharynx. Encephalitic symptoms.
M. S.	3 yr.	F	White	Died on 4th day, day of admission.	Subcortical—paralysis of larynx and pharynx. Died in respirator.
D. G.	5 yr.	F	Black	Died on 4th day, day of admission.	Encephalitic
D. C.	11 yr.	M	White	Died on 8th day, two days after admission.	Subcortical—paralysis of larynx and pharynx. Died in respirator.

CLINICAL PICTURE

One gathers from the data presented how difficult it would be to reconstruct a typical case of poliomyelitis. There was no one sign pathognomonic of this disease. However, the occurrence of certain of the more classical symptoms in a patient would suggest such a diagnosis. No symptom or sign noted in our series was present in every case. About 10 per cent had no fever. Seven of the eighty-two patients whose spinal fluids were examined had normal cell counts, and six of these showed no increase of the globulin content.

The more important symptoms to be elicited are moderate fever associated with upper respiratory tract infection, gastrointestinal symptoms, muscular weakness, and a feeling of malaise. The more common gastrointestinal symptoms to be expected are anorexia, nausea, vomiting, and constipation, in other words, disturbances of the gastrointestinal tract which are usually found in most of the infections of childhood. The malaise may be of a moderate degree or so profound as to leave the patient in a state of complete exhaustion. Profuse sweating is common in this latter state. This severe degree of intoxication was seen only in the early part of the disease. In many in-

stances, because of the marked generalized muscular relaxation, it was impossible during this stage to determine the extent of paralysis. With recovery from this acute exhaustion, it was often discovered that no true paralysis had existed. Headache and backache are commonly present. The patient may be either drowsy or irritable. At times the irritability is noticed only when the patient is disturbed. Early in the disease hyperesthesia is a common complaint. This may be generalized or limited to the spine but most commonly is in regions where paralysis is later to occur. Muscular tenderness is sometimes brought out by passive motion when there is no complaint of pain. In the nonparalytic cases hyperesthesia is of a more transient nature.

In the diagnosis of poliomyelitis there are several points in the physical examination that are of extreme importance. Hyperesthesia, as described above, is frequent. Alteration of the reflexes is found in the majority of instances. However, this is not always associated with paralysis even though the reflex may be entirely absent. Palsy is not likely to develop in the absence of reflex changes. Stiff neck is an early and frequent sign. Associated with this in about half the cases one finds a head drop, which can be detected by elevating the patient's shoulders while he is flat on his back. When head drop is present, the patient is unable to bring his head up from the bed or does so very weakly. This symptom we have found to be of considerable help in detecting some of the more obscure cases. Stiffness of the back associated with pain on flexion is also an early symptom in a large number of cases. This can be demonstrated by having the patient sit on a bed with his feet extended and having him flex his trunk bringing his head toward his legs. The average normal child can almost touch his legs with his head while in this position.

Muscular paralysis, which may be limited to a single muscle group or which may be so extensive as to involve the entire body, is the most classical sign. However, it is to be remembered that over half of the patients do not develop paralysis. In fact, all the neuromuscular symptoms may be absent. In many of the cases the paralysis comes on suddenly and is complete. In other cases it is progressive over several days; in these latter cases there is usually a continued fever. As long as the fever continues, it is possible that the paralysis may spread. The localization of the paralysis differs in different epidemics. The more usual localization is in the legs. Cranial nerve palsy is sometimes found. The more common of these are the oculomotor, the facial, and the spinal accessory. Other central nervous system symptoms are occasionally encountered, such as convulsions, respiratory disturbances, and disturbances of swallowing.

The chief diagnostic laboratory aid is obtained from examination of the spinal fluid, which is characterized by an increased globulin content and cell count. Early in the disease the predominating cell may be a

polynuclear cell. Soon, however, lymphocytes predominate. The average count is between 75 and 200. However, there is considerable variation. As mentioned above, a normal spinal fluid may be present. In the majority of instances the fluid is colorless and clear, but occasionally it is opalescent.

The white blood cell count shows a slight increase averaging around 10,000, occasionally over 15,000 and often under 7,000. The differential count shows the polynuclear cells slightly increased.

TREATMENT

In addition to the symptomatic treatment administered to each of these cases, e.g., hypertonic solutions intravenously to patients exhibiting encephalitic symptoms, sedatives, etc., the majority of the patients received a blood transfusion and serum on admission. The serum, obtained from the Philadelphia Department of Public Health, was either contact or convalescent. It was not tested for its antiviral potency. Blood was obtained from parents. Serum was always given intramuscularly, except in two instances when it was injected intravenously. The number of patients receiving serum therapy is given in Table VII. We

TABLE VII

TREATMENT	NO. RECEIVING THERAPY
Transfusion (indirect)	49
Nonparalyzed	29
Paralyzed	20
Serum	73*
Nonparalyzed	39
Paralyzed	34
Average dose of convalescent serum	36.3 c.c.
Average dose of contact serum	39.6 c.c.

*Some of these patients also received a blood transfusion.

are unable to evaluate the worth of this form of therapy since no effort was made to control its administration, blood and serum being given to paralyzed and nonparalyzed patients alike. However, in eleven cases (Table VIII) convalescent and contact serum, plus the administration of an intravenous blood transfusion in the preparalytic stage of the disease, did not prevent the development of paralysis. Two of these patients showed mild weakness before serum was given but developed further paralysis after treatment. The fact that five of these patients had treatment for at least four days before the paralysis developed again raises the question whether the use of convalescent serum after or very shortly before the onset of the disease is of any benefit. Of course, these particular serums may have had only little antiviral potency. The orthopedic aspect of the treatment will not be discussed in this paper.

TABLE VIII

OCCURRENCE OF PARALYSIS FOLLOWING SERUM THERAPY IN THE PREPARALYTIC STAGE OF DISEASE

	C.C. OF CONVALESCENT SERUM	C.C. OF CONTACT SERUM	BLOOD TRANS.	PARALYSIS DEVELOPED	
				DAYS AFTER ADMINISTRATION	DAYS AFTER ONSET OF DISEASE
B. H.	25	50	Blood trans.	2	3
R. M.	25	40	Blood trans.	5	8
P. B.	10	45	Blood trans.	5	6
W. G.	40	10	Blood trans.	5	7
J. S.	50	--	Blood trans.	5	8
R. C.	20	40	Blood trans.	2	7
J. A.	45	20	Blood trans.	3	6
W. B.	25	30	Blood trans.	1	4
W. B.	--	50	Blood trans.	2	3
M. G.	20	40	Blood trans.	1	4
M. C.	50	40	Blood trans.	4	8

The prophylactic use of serum in the treatment of poliomyelitis is discussed in another paper published from this clinic.

SUMMARY

1. An analysis is presented of the data taken from the records of 100 cases of acute poliomyelitis.

2. The maximum number of patients were hospitalized during the last week of August and the first week of September, 1932. With the ages of the patients varying from one to twelve years, 51 per cent of the patients were between one and one-half and five years of age. Males predominated over females in the ratio of 1.22 to 1. Color did not seem to confer any immunity. The majority of the patients in this series were well-nourished, well-developed children with normal hemoglobin concentration. The blood types of the patients had no influence on the incidence. Four patients who had received intramuscular whole blood as an attempted prophylactic measure did not develop paralysis but did develop the disease.

3. A discussion of the classification of the types of cases is presented.

4. Symptoms:

A. Fever: Most patients exhibited fever on admission, ranging between 100° and 102° F. The dromedary type of temperature curve was not encountered.

B. Gastrointestinal: Constipation, nausea, vomiting, and anorexia were frequent symptoms. Abdominal pain was not uncommon. Diarrhea of a mild type occurred occasionally.

C. Cardiorespiratory: An initial upper respiratory infection occurred in a high percentage of cases. Respiratory phenomena incident to paralysis are discussed. Cardiovascular abnormalities were present.

D. General: Deep pressure pain occurred in the majority of cases, as a transient symptom in nonparalytic cases and as a protracted symptom in those developing paralysis. Drowsiness appeared early in more than half the cases. Headache and backache occurred in 46.6 per cent and 26.6 per cent, respectively, of children able to give evidence of them. Irritability, weakness, and toxicity were rather frequent; restlessness and sweating were occasional occurrences; convulsions were rare.

E. Nervous: Nuchal rigidity, stiffness of the back, and head drop were common early occurrences. Trophic and vasomotor disturbances were occasionally met.

F. Genitourinary: Urinary retention occurred in less than 10 per cent of the patients as a transient symptom.

G. Glandular: In no case was there generalized lymphadenopathy or splenic enlargement.

H. Paralysis: A detailed analysis of the incidence, distribution, and relationship of reflexes to muscle paralysis is made.

5. Laboratory Data:

A. Spinal Fluid: The fluid was usually clear and colorless. Pleocytosis was almost uniformly encountered. The relationship of the pleocytosis to paralysis and its variation during the course of the disease is outlined. Globulin was found increased in most of the fluids examined. An increase in the sugar content was found in but 23 per cent of the cases, the remaining patients exhibiting spinal fluid sugars within normal range. Chlorides were almost always normal. The Wassermann reaction carried out in twenty-five cases was negative. The fluids of nine patients showed slight pelliele formation.

B. Urine: Urinary findings were those of any febrile disturbance.

C. Serology: The blood Wassermann reaction determined in twenty-four patients was positive in one case—this a known case of syphilis.

D. Hematology: The leucocytic response to the disease is analyzed.

6. The total mortality rate in this series was 7 per cent. However, in those children under eighteen months of age the mortality was 25 per cent.

7. The therapeutic measures employed in the early treatment of these cases are tabulated.

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CLINICAL EXPERIENCE WITH CRYSTALLINE VITAMIN D: THE INFLUENCE OF THE MENSTRUUM ON THE EFFECTIVENESS OF THE ANTIRACHITIC FACTOR

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IN 1931, Askew and his colleagues[1] in England and Windaus and his coworkers[2] in Germany, employing different chemical methods, finally isolated from irradiated ergosterol a pure crystalline substance which has marked antirachitic activity. Windaus named this crystalline product "vitamin D_2," and the English investigators called it "calciferol." It has been fairly well established that vitamin D_2 and calciferol are identical substances, and we shall refer to them in this paper as "crystalline vitamin D." Windaus and Leuttringhaus[3] have isolated a number of other substances which occur during the course of irradiation of ergosterol, and it is interesting to note that none of them has any antirachitic activity. They are all isomers of ergosterol and have been designated as "lumisterol," "tachysterol," "suprasterol 1 and 2," and "substance 248" (toxisterol).

One milligram of crystalline vitamin D has a potency of 40,000 international units (approximately 14,815 Steenbock units). Crystalline vitamin D, being an isomer of ergosterol, has the chemical formula of $C_{28}H_{44}O$. It is dextrorotatory and has a melting point of 114° to 115° C. and an intense absorption band at 265 mu. The pure vitamin is extraordinarily stable, being resistant to oxidation and showing no loss of potency after storage for five months at 20° and at 37° C. or after heating for nine hours at 115° C.

Crystalline vitamin D as well as tachysterol and substance 248 are toxic to rats and mice when given in large amounts. The margin of safety, however, is great, inasmuch as toxic effects occur only after the administration of 3,000 times the therapeutic dose of crystalline vitamin D.

Clinical tests of the antirachitic value of crystalline vitamin D have been carried out abroad by Spence[4] and by Gorter.[5] Spence observed the effect of the daily administration of 1 c.c., 2 c.c. and 3 c.c. of an oily solution of crystalline vitamin D on the course of the disease in twelve patients with active rickets, ranging in age from one to eighteen years. One cubic centimeter of this preparation contained 3,000 international units (1,111 Steenbock units). In all

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This work was planned with Dr. A. F. Hess but was carried out and written after his death.

twelve cases definite healing was noted on the roentgenograms by the end of the fourth week, and complete healing was observed within thirteen weeks. Gorter places the daily curative dose of crystalline vitamin D at 0.05 mg., in other words at 2,000 international units (740 Steenbock units).

The discrepancy between the rat unit potency and the clinical effectiveness of various antirachitic agents constitutes one of the most interesting problems in the therapeutics of rickets. For example, it has been shown that 42 rat units (Steenbock units) in the form of irradiated milk protect against or cure infantile rickets, whereas 80 units in the form of milk from cows fed irradiated yeast and from 600 to 800 units in the form of viosterol are necessary to bring about similar results. The ratio of effectiveness of irradiated milk, "yeast" milk, and viosterol from the standpoint of rat units is approximately 15:8:1.[6]

In view of the fact that irradiated milk and milk from cows fed irradiated yeast require fewer units than viosterol to protect against or cure infantile rickets, the question arose as to whether the medium of milk may allow for better utilization of the antirachitic vitamin in infants than does the medium of oil. In order to test the validity of this hypothesis, it was decided to give one group of rachitic infants daily 90 units (Steenbock units) of crystalline vitamin D dissolved in oil and another group a similar number of units of the antirachitic factor incorporated in milk and to compare the healing in both groups of infants. A potency of 90 units was chosen because it is known from experience with viosterol and from available reports in the literature concerning the curative dose of crystalline vitamin D that this dosage in units in oil would be inadequate to cure a large percentage of rachitic infants. On the other hand, 90 units incorporated in milk should prove to be effective if the supposition were correct that the menstruum of milk was responsible for the lower number of units in the form of irradiated milk or of "yeast" milk required to cure rickets.

Accordingly nine infants showing evidences of rickets on roentgenographic examination were given daily 90 units of crystalline vitamin D incorporated in 24 ounces of milk; and another group of nine infants, comparable from the standpoint of age, severity of rickets, and daily intake of milk, were given 90 units of crystalline vitamin D dissolved in six drops of corn oil. These infants were enrolled in various health stations in New York City; I am indebted to the commissioner, Dr. John L. Rice, for his cooperation in connection with this study. The rachitic infants were followed up carefully in their homes and in the clinics throughout the test period, which began early in January and ended late in April. A special nurse was assigned to this investigation and the babies were seen by her on an average of twice a

week. It should be added that only those babies whose mothers were cooperative and could be relied upon to follow instructions were included in the study.

After the infants had received crystalline vitamin D in milk or in oil for four weeks, roentgenograms were again taken of their wrists in order to determine the degree of healing which had taken place during this period. As emphasized in previous publications, the employment of the four-week test period is a good method of evaluating the relative potencies of antirachitic agents. In order to determine the progress of healing, however, roentgenograms were taken, when possible, after the infants had received crystalline vitamin D for six, eight, and ten weeks.

If milk were found to play a rôle in bringing about better utilization of the antirachitic factor, it would be of interest to know the minimum curative dose of crystalline vitamin D incorporated in milk. Thus we might learn whether milk to which the antirachitic factor has been directly added resembles, from the point of view of the number of units required to cure rickets, irradiated milk or milk from cows fed irradiated yeast. Accordingly, eight rachitic infants were given daily 45 units of crystalline vitamin D incorporated in 24 ounces of milk, a potency which is known to be adequate for irradiated milk but inadequate for "yeast" milk.

The scope of the investigation was further enlarged to determine the effect on the course of active rickets of a larger amount of crystalline vitamin D dissolved in oil. Ten rachitic infants were therefore given daily 6 drops of an oily preparation of crystalline vitamin D totaling 900 Steenbock units.

This study therefore comprised thirty-six rachitic infants divided into four groups: (1) nine infants receiving daily 90 units of crystalline vitamin D dissolved in oil; (2) nine infants receiving 90 units incorporated in milk; (3) eight infants receiving 45 units of crystalline vitamin D incorporated in milk, and (4) ten infants receiving 900 units of crystalline vitamin D dissolved in oil.

The incorporation of crystalline vitamin D in milk was accomplished either by (1) the "vipro" process, as advocated by Laquer,[7] consisting of the addition of an oily preparation of vitamin D to dry skimmed milk which is then mixed with fluid milk, or (2) by dissolving crystalline vitamin D in propylene glycol* and adding this solution directly to milk. By means of these methods, crystalline vitamin D is uni-

*Hunt (J. Indus. & Engin. Chem. 24: 361, 1932) has shown propylene glycol to be relatively nontoxic and states that it may have a true food value in the sense that ethyl alcohol does without the drug action of the latter. Young rats grew at the normal rate and reached maturity when the only liquid they received was a 5 per cent solution of propylene glycol. It was also well tolerated by animals whose livers and kidneys had been injured by various poisons.

Propylene glycol is miscible with milk and water in all proportions and forms stable solutions of crystalline vitamin D. The taste and odor of milk are not altered by the addition of therapeutic amounts of crystalline vitamin D propylene glycol solution.

formly distributed throughout the milk, a fact which has been demonstrated by biologic assays of various levels of milks so treated. The vipro method was used for the preparation of milk of weaker potency, namely 45 units in 24 ounces of milk, and the propylene glycol solution for the incorporation of 90 units of crystalline vitamin D in 24 ounces of milk. The practical advantage of a propylene glycol solution of crystalline vitamin D is that it mixes freely with the milk, whereas drops of an oily solution cannot be distributed uniformly through milk unless the vipro process is employed.

The preparations of crystalline vitamin D were kindly sent to us by Dr. Charles W. Hooper. The incorporation of crystalline vitamin D was carried out daily shortly before delivery of the milk. Biologic assays of the milk and of the oily preparations of crystalline vitamin D used in this investigation were made three times during the course of the investigation, and the results showed that the requisite number of units were contained therein.

RESULTS

The results of this study may be gleaned from Table I. In surveying the data, it will be noted that at the end of four weeks all of the nine rachitic infants receiving daily 90 units of crystalline vitamin D in milk showed definite healing, whereas only three of nine rachitic infants receiving 90 units of crystalline vitamin D in corn oil showed healing. It should be added that the gains in weight in both groups were approximately the same.

At the end of six weeks healing progressed in those infants receiving the antirachitic vitamin in milk, and in one instance the lower ends of the radius and ulna were normal. We were able to obtain roentgenograms of six infants who had received crystalline vitamin D in milk for eight weeks, and in four of them the bones were normal, and in the other two infants rickets was either healed or almost healed (Figs. 1, 2, 3, 4). In contrast to these favorable results with crystalline vitamin D in milk, three of the eight infants receiving daily 90 units of crystalline vitamin D in oil for six weeks showed no healing and at the end of eight weeks the rachitic process became worse in two instances (Figs. 5, 6, 7).

One rachitic infant (B. R.) is of especial interest and significance. This baby had received 90 units of crystalline vitamin D in oil for four weeks, and roentgenographic examination at the end of this period showed that the rachitic process advanced. This infant was then given the same number of units of crystalline vitamin D in milk and, as will be noted in Fig. 8, definite healing resulted in four weeks and calcification in the rachitic zone was increased two weeks later.

It is obvious that 90 units of crystalline vitamin D in the form of propylene glycol solution incorporated in milk was much more ef-

TABLE I

COMPARISON OF HEALING, AMONG 36 RACHITIC INFANTS, BROUGHT ABOUT BY CRYSTALLINE VITAMIN D INCORPORATED IN MILK OR IN CORN OIL

CASE	AGE (MO.)	DATE BEGUN	MENSTRUUM IN WHICH CRYSTALLINE VITAMIN D WAS INCORPORATED	NO. OF RAT UNITS (STEENBOCK) GIVEN	ROENTGENOLOGIC RICKETS					COMMENT
					AT ONSET	HEALING AFTER 4 WK.	HEALING AFTER 6 WK.	HEALING AFTER 8 WK.	HEALING AFTER 10 WK.	
C. M.	8	1/23	Milk†	45	Moderate	+	++	+++	++++	Porto Rican
B. G.	6	1/25			Moderate	+	+±	++	++±	Porto Rican
F. S.	13	1/26			Moderate	0	0			Negro
E. D.	6	2/ 7			Slight	+	++	+++±		Italian
G. N.	8	2/18			Moderate	+	+±	++	+++	Porto Rican
C. W.	22	2/17			Marked	+±	++	++±		Negro
G. B.	8	2/21			Moderate	+±	++±	+++±		Negro
J. N.	6	2/24			Mild	0	0	0 (worse)		Negro
V. L.	6	1/13	Milk‡	90	Slight	++	+++	Normal		Italian
S. Q.	4	1/13			Moderate	+±	++±	+++±	++++	Porto Rican
J. A.	5	1/13			Slight	+++	++++	Normal		Negro
R. L.	5	1/19			Moderate	+++	Normal	Normal	Normal*	Negro
C. H.	20	1/25			Marked	+++	+++±	++++	Normal	Negro—1/25: calcium, 9.8 mg.; phosphorus, 3 mg. 2/23: calcium, 10.6 mg.; phosphorus, 5 mg.
K. S.	4	2/22			Slight	++	+++	Normal		Negro
B. C.	7	3/ 2			Moderate	+				Porto Rican
F. S.	15	3/17			Moderate	+	+±			Negro
B. R.	6	3/17			Moderate	+±	+++			This infant had received 90 units of crystalline vitamin D in oil for one month, and no healing resulted

+Denotes slight healing; ++, moderate healing; +++, marked healing; ++++, healed rickets.

* X-ray picture taken at 13 weeks.

†One liter contained 60 units.

‡One liter contained 120 units.

TABLE I—CONT'D

CASE	AGE (MO.)	DATE BEGUN	MENSTRUUM IN WHICH CRYSTALLINE VITAMIN D WAS INCORPORATED	NO. OF RAT UNITS (STEENBOCK) GIVEN	ROENTGENOLOGIC RICKETS					COMMENT
					AT ONSET	HEALING AFTER 4 WK.	HEALING AFTER 6 WK.	HEALING AFTER 8 WK.	HEALING AFTER 10 WK.	
T. R.	5	2/ 4	Oil§	90	Moderate	+±	++±	+++	++++	Porto Rican
S. L.	7	2/12			Slight	?	+	+±		
B. M.	4	2/14			Slight	+	++		++	Negro
B. R.	5	2/16			Slight	0 (worse)				Negro
V. B.	14	2/16			Marked	+	+±	++	+++	Negro
D. R.	7	2/21			Moderate	0	0	0 (worse)	0	Negro
C. Q.	5	2/23			Slight	?	+	+±	++±	Porto Rican
C. B.	8	2/28			Moderate	0	0	0 (worse)		Negro
T. B.	8	3/19			Moderate	0	0			Negro
J. B.	3	2/16	Oil‖	900	Slight	++		Normal	Normal	Negro
P. G.	6	2/ 9			Slight	++	++++			Italian
J. B.	6	2/16			Slight	++	++±	+++	+++±	Negro
T. B.	6	2/16			Slight	++	++++	Normal		Negro
C. M.	6	2/16			Moderate	++				Negro
R. P.	17	2/17			Marked	+				Negro
H. B.	4	2/17			Slight	++	+++	+++±	Normal	Negro
J. D.	7	2/17			Moderate	++	++±	+++	+++±	Negro
N. E.	3	2/17			Slight	+	++	++±		2/15: calcium, 7.2 mg.; phosphorus, 5.3 mg. 3/13: calcium, 10.3 mg.; phosphorus, 6.1 mg.
J. D.	24	1/30			Marked	+	+	+	+±	Negro; at 12 weeks healing ++

§One drop contained 15 units.
‖One drop contained 150 units.

fective than the same number of units in oil. These results clearly indicate that the medium of milk allows for better utilization of the

Fig. 1.—(C. H.) Healing of rickets brought about by crystalline vitamin D (90 units) in milk; *A*, January 25 (begun); *B*, February 21 (four weeks later); *C*, March 8 (two weeks later); *D*, March 21 (two weeks later); *E*, April 24 (five weeks later).

Fig. 2.—(R. L.) Healing of rickets brought about by crystalline vitamin D (90 units) in milk: *A*, January 19 (begun); *B*, February 15 (four weeks later); *C*, March 5 (two and one-half weeks later); *D*, March 29 (three and one-half weeks later).

antirachitic vitamin than does the medium of corn oil, and thus offer an explanation for the greater effectiveness, from the standpoint of rat units, of antirachitic milks as a group as compared with viosterol.

Of the eight infants who received daily 45 units of crystalline vitamin D in 24 ounces of milk, six showed definite healing at the end of four weeks. At six weeks healing progressed in these six infants, and after eight weeks roentgenographic examination revealed further

Fig. 3.—(S. Q.) Healing of rickets brought about by crystalline vitamin D (90 units) in milk; *A*, January 13 (begun); *B*, February 9 (four weeks later); *C*, February 27 (two and one-half weeks later); *D*, March 14 (two weeks later); *E*, March 26 (two weeks later).

Fig. 4.—(J. A.) Healing of rickets brought about by crystalline vitamin D (90 units) in milk; *A*, January 13, (begun); *B*, February 9 (four weeks later); *C*, February 27 (two and one-half weeks later); *D*, March 14 (two weeks later).

healing; in two instances the rachitic disorder was almost healed. Two infants, however, failed to show healing at the end of four and six weeks, and in one infant followed for eight weeks the rickets became worse. One baby (F. S.), who showed no healing after having received 45 units in milk for six weeks, was given 90 units in milk for

four weeks, and at the end of this period definite healing was noted on the roentgenogram.

It is evident that the results with 45 units of crystalline vitamin D in milk were superior to those obtained with 90 units of crystalline

Fig. 5.—(C. B.) Absence of healing with crystalline vitamin D (90 units) in corn oil; *A*, February 28 (begun); *B*, March 29 (four weeks later); *C*, April 12 (two weeks later); *D*, April 27 (two weeks later).

Fig. 6.—(D. R.) Absence of healing with crystalline vitamin D (90 units) in corn oil; *A*, February 21 (begun); *B*, March 21 (four weeks later); *C*, April 4 (two weeks later); *D*, April 18 (two weeks later); *E*, April 30 (two weeks later).

vitamin D in oil. However, in view of the fact that healing was not brought about in two of eight infants, this unitage in milk must be considered inadequate for curative purposes.

From these experiences it would seem that milk which had been fortified with crystalline vitamin D resembled more closely milk produced from cows fed irradiated yeast rather than irradiated milk, in-

asmuch as 45 units of crystalline vitamin D failed to cure all of the eight rachitic infants, whereas 90 units proved adequate.

At first glance, it would seem that the increased effectiveness of crystalline vitamin D when incorporated in milk as compared with its administration in oil might be due to better absorption of vitamin D in the intestinal tract when the antirachitic factor is administered in milk. However, biologic assays of the feces of two infants who had been receiving 90 units of crystalline vitamin D in milk and of the

Fig. 7.—(T. B.) Absence of healing with crystalline vitamin D (90 units) in corn oil: *A*, March 17 (begun); *B*, April 19 (four and one-half weeks later); *C*, May 1 (one and one-half weeks later).

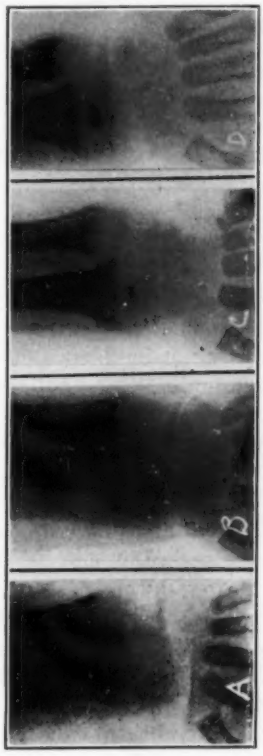

Fig. 8.—(B. R.) Absence of healing with crystalline vitamin D (90 units) in corn oil; healing brought about by crystalline vitamin D (90 units) in milk: *A*, February 16 (oil begun); *B*, March 18 (milk begun); *C*, April 17 (four weeks later); *D*, April 30 (two weeks later).

feces of two infants who had been receiving 90 units of crystalline vitamin D in oil for the same period showed approximately the same amount of vitamin D. Samples of blood were also taken from these infants for assay of vitamin D in order to determine whether there was an increase of the antirachitic factor in the blood of those receiving crystalline vitamin D in milk. The results of this experiment revealed that there was no difference in the vitamin D content of the blood in both groups of infants. The superior utilization of crystalline vitamin D when administered in the menstruum of milk does not seem, therefore, to be due to better absorption of the antirachitic factor in the intestinal tract, but a final decision concerning the rôle of absorption

in connection with this interesting phenomenon must be held in reservation until assays of the blood and feces of a larger number of infants are carried out.

RESULTS WITH 900 STEENBOCK UNITS OF CRYSTALLINE VITAMIN D IN OIL

Ten rachitic infants, ranging in age from three to twenty-four months, were given daily 6 drops of crystalline vitamin D in oil, one drop containing 150 (Steenbock) units. One baby had manifest tetany; and the calcium content of the blood was 7.3 mg., and the inorganic phosphorus 6.1 mg. per 100 c.c. As will be observed in Table I, healing was noted on the roentgenograms in every instance at the end of four weeks, and the calcium content of the blood of the infant with tetany was normal, 10.3 mg. per 100 c.c. of blood. At the end of eight weeks, two of seven infants showed normal bones on roentgenographic examination and the other five infants revealed from slight to marked healing. However, one negro baby who had marked rickets was followed for twelve weeks, and at the end of this period only slight to moderate healing was observed. The impression gained from these experiences is that 900 units of crystalline vitamin D in oil is a good therapeutic dose for mild or moderate cases of rickets, but may not be adequate for severe cases. The therapeutic results with 90 units of crystalline vitamin D in milk were superior to those obtained with 900 units in oil.

We used approximately a 450-D preparation of crystalline vitamin D in oil but would advise that commercially a 250-D preparation should be supplied in order to conform with the present potency of viosterol (250-D). For mild and moderate cases of rickets from 10 to 15 drops of crystalline vitamin D in oil (250-D) should be given, and for marked cases, from 20 to 60 drops daily. It may be noted that these recommended curative doses of crystalline vitamin D in oil are the same as those generally advised for viosterol. One can readily understand the similarity in behavior of crystalline vitamin D in oil and viosterol when it is recalled that crystalline vitamin D is obtained from irradiated ergosterol and this accounts for the entire antirachitic potency of irradiated ergosterol.

The advantage of the use of pure crystalline vitamin D is that it obviates the necessity to some extent of biologic assays, as 1 mg. of crystalline vitamin D has a uniform potency of 40,000 international units. However, biologic assays should be carried out from time to time as a check on the accuracy of the technic employed in the preparation of solutions of crystalline vitamin D.

SUMMARY

In order to determine whether crystalline vitamin D in milk was more effective unit for unit than crystalline vitamin D in oil, nine

rachitic infants were given 90 units of crystalline vitamin D in milk, and nine were given 90 units of crystalline vitamin D in oil and a comparison of healing in both groups was noted. The scope of the investigation was enlarged to include a study of the effect on the course of rickets of 45 units of crystalline vitamin D in milk, and 900 units in oil. Accordingly eight rachitic infants were given daily 45 units of crystalline vitamin D in milk, and ten infants, 900 units in oil.

The results of the administration of 90 units of crystalline vitamin D in milk were definitely superior to those obtained with a similar number of units in oil. Of nine infants receiving 90 units of crystalline vitamin D in milk, healing was observed in all at the end of one month, whereas only three of nine infants receiving 90 units of crystalline vitamin D in oil showed healing during the same period of observation. Roentgenograms were also taken after crystalline vitamin D had been given for six, eight, and ten weeks, and the results revealed that the group of infants receiving the antirachitic vitamin in milk reacted more favorably. These results indicate that the medium of milk allows for better utilization of the antirachitic vitamin than does the medium of corn oil and thus offer an explanation for the greater effectiveness, from the standpoint of rat units, of antirachitic milks as compared with viosterol.

The therapeutic results with 45 units of crystalline vitamin D in milk were superior to those obtained with 90 units of crystalline vitamin D in oil. However, two failures were noted among eight infants receiving the 45-unit milk, so that this dosage of units in milk must be regarded as below the therapeutic level.

With 900 units of crystalline vitamin D in oil, satisfactory healing resulted in nine of ten rachitic infants. We would recommend that from 10 to 15 drops (800 to 1,200 Steenbock units) of a 250-D preparation of crystalline vitamin D in oil should be used as a curative dose for mild and moderate cases of rickets and that from 20 to 60 drops be given for marked cases. However, if a solution of crystalline vitamin D in propylene glycol 250-D is employed by incorporation in 24 ounces of milk, only one drop (83 Steenbock units) is necessary to cure infantile rickets.

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OBSERVATIONS ON THE PRESENCE OF COMPLEMENT IN THE CEREBROSPINAL FLUID IN VARIOUS PATHOLOGIC CONDITIONS OF THE CENTRAL NERVOUS SYSTEM

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DURING the course of studies on meningitis due to *B. influenzae*, it became of some interest to gather data regarding the presence of complement in the cerebrospinal fluid of patients suffering from various etiologic types of acute inflammatory disease of the meninges and central nervous system. It has long been known that complement is not present in normal cerebrospinal fluid. A few observations have been recorded regarding complement in the cerebrospinal fluid in meningitis. Davis[1] in 1905 noted its absence in a study of five cases of meningococcus meningitis. M'Kenzie and Martin[2] in 1908 noted its absence in a few cases of meningococcus meningitis. In 1918 Kolmer, Toyama, and Matsunami[3] reported a small group of cases of meningococcus, pneumococcus, and aseptic meningitis. They found complement to be absent in the cerebrospinal fluid of the majority of these cases, although it was present in an occasional instance of each of these types of meningitis. Ward and Fothergill[4] and Ward and Wright[5] have commented on the absence of complement in the cerebrospinal fluid in meningitis due to *B. influenzae*. They suggested that complement might be an essential factor in the serum treatment of this disease. In a recent article on *B. influenzae* meningitis, Neal, Jackson, and Appelbaum[6] state: "There is a certain vogue at present for adding complement to the serum in treating cases of influenza bacillus meningitis. From a theoretical standpoint and from the results in certain cases under our observation, we fail to see that it is of any value." Neither theoretical argument nor experimental evidence to support this statement is given by these authors.

There have been several reports concerning the use of complement in the treatment of meningococcus meningitis. M'Kenzie and Martin[2] treated sixteen acute cases with convalescent and patient's serum intrathecally and had ten recoveries. In 1916 Fairley and Stewart[7] added fresh human (convalescent) serum to antimeningococcus serum before intraspinal administration and reported seven recoveries out of ten acute cases thus treated.* In these reports the destruction of organisms probably was due to a specific immune body although complement may

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Aided by the Philip Ellis Stevens, Jr., Memorial Gift.

*Quoted from Bunim and Wies. The author has been unable to secure the original report of Fairley and Stewart.

have played a rôle. Recently Bunim and Wies[8] have reported the successful termination of meningococcus meningitis in a patient only after the administration of complement. Their patient was an eight-and-one-half-year-old girl who was treated intensively with a specific serum of high agglutinating titer. The cerebrospinal fluid continued to yield positive cultures. After twenty-eight successive positive cultures the patient was given a single large dose (15 c.c.) of complement followed by additional antimeningococcus serum. This treatment was followed by immediate sterilization of the cerebrospinal fluid with complete recovery. These authors also quote a personal communication from Kolmer in which he reports the successful application of this principle in the treatment of five cases.

With regard to meningitis due to *B. influenzae* Ward and Fothergill[4] reported five cases treated with specific antiserum and complement. In some of these patients the cerebrospinal fluid was temporarily sterilized and some benefit could be ascribed to the treatment although there were no eventual recoveries. The more recent experiences of these authors in the treatment of this disease will be reported in the near future. Pittman[9] has used complement in the treatment of a few cases but was unable to see any practical value in its use. Recently Rittenberg[10] has reported a single case of *B. influenzae* meningitis, in an eight-year-old girl who recovered completely following the intrathecal administration of complement and *B. influenzae* antiserum.

In the present study the cerebrospinal fluid of seventy-one patients with various types of acute inflammatory disease of the central nervous system has been tested for complement. In many of these patients the cerebrospinal fluid was tested for complement repeatedly during the course of meningococcus and *B. influenzae* meningitis and its treatment.

Technic.—The tests for complement were made as soon as possible (usually within one to two hours) after the withdrawal of cerebrospinal fluid from the patient. Whenever the test could not be performed immediately, the fluid was stored in the ice box (10° C.). It was found that storage overnight in the refrigerator did not appreciably alter the complement content. Before testing, the cerebrospinal fluid was centrifuged at high speed in order to separate all cellular material. The clear supernatant fluid was used in the test. Specimens containing blood (resulting from traumatic lumbar puncture, etc.) were discarded because of the possibility of contaminating the fluid with complement from the patient's serum. The presence of blood was easily detected by noting the presence of erythrocytes in the sedimented material after centrifuging.

One cubic centimeter amounts of cerebrospinal fluid and its dilutions were used. To the first of seven tubes 1 c.c. of cerebrospinal fluid was added. Serial dilutions of cerebrospinal fluid in physiologic salt solution in total volumes of 1 c.c. were placed in the remaining tubes. The

TABLE I

COMPLEMENT IN THE CEREBROSPINAL FLUID

CASE	DIAGNOSIS	DILUTION OF CEREBROSPINAL FLUID						
		0	1:2	1:4	1:8	1:16	1:32	1:64
1	Meningococcus meningitis	0	0	0	0	0	0	0
2	Meningococcus meningitis	0	0	0	0	0	0	0
3	Meningococcus meningitis	+	0	0	0	0	0	0
4	Meningococcus meningitis	++++	++++	++	0	0	0	0
5	Meningococcus meningitis	++++	++	0	0	0	0	0
6	Meningococcus meningitis	0	0	0	0	0	0	0
7	Meningococcus meningitis	0	0	0	0	0	0	0
8	Meningococcus meningitis	++++	++	0	0	0	0	0
9	Meningococcus meningitis	0	0	0	0	0	0	0
10	Meningococcus meningitis	0	0	0	0	0	0	0
11	Meningococcus meningitis	0	0	0	0	0	0	0
12	Meningococcus meningitis	++++	++++	++++	++	+	0	0
13	Meningococcus meningitis	0	0	0	0	0	0	0
14	Aseptic meningitis	++++	+++	+	0	0	0	0
15	Aseptic meningitis	0	0	0	0	0	0	0
16	Aseptic meningitis	++++	+++	0	0	0	0	0
17	Pneumococcus meningitis	0	0	0	0	0	0	0
18	Pneumococcus meningitis	0	0	0	0	0	0	0
19	Pneumococcus meningitis	++++	+++	++	0	0	0	0
20	Pneumococcus meningitis	0	0	0	0	0	0	0
21	Tuberculous meningitis	++++	++++	++	0	0	0	0
22	Tuberculous meningitis	++++	++	0	0	0	0	0
23	Tuberculous meningitis	++	+	0	0	0	0	0
24	Hemolytic streptococcus meningitis	++++	++++	++++	++++	++++	++++	++++
25	Hemolytic streptococcus meningitis	++	0	0	0	0	0	0
26	Hemolytic streptococcus meningitis	++++	++++	++	+	0	0	0
27	Hemolytic streptococcus meningitis	++++	++	0	0	0	0	0
28	Hemolytic streptococcus meningitis	++++	++	0	0	0	0	0
29	Hemolytic streptococcus meningitis	++++	++++	++	0	0	0	0
30	Poliomyelitis	0	0	0	0	0	0	0
31	Poliomyelitis	0	0	0	0	0	0	0
32	Bulbar poliomyelitis	++	0	0	0	0	0	0
33	Poliomyelitis	0	0	0	0	0	0	0
34	Bulbar poliomyelitis	0	0	0	0	0	0	0
35	Influenzal meningitis	0	0	0	0	0	0	0
36	Influenzal meningitis	0	0	0	0	0	0	0
37	Influenzal meningitis	+++	+	0	0	0	0	0
38	Influenzal meningitis	0	0	0	0	0	0	0
39	Influenzal meningitis	0	0	0	0	0	0	0
40	Influenzal meningitis	0	0	0	0	0	0	0
41	Influenzal meningitis	0	0	0	0	0	0	0
42	Influenzal meningitis	++++	++	+	0	0	0	0
43	Influenzal meningitis	0	0	0	0	0	0	0
44	Influenzal meningitis	0	0	0	0	0	0	0
45	Influenzal meningitis	0	0	0	0	0	0	0
46	Influenzal meningitis	++++	++++	++	0	0	0	0
47	Influenzal meningitis	0	0	0	0	0	0	0
48	Influenzal meningitis	0	0	0	0	0	0	0
49	Influenzal meningitis	+++	0	0	0	0	0	0
50	Influenzal meningitis	0	0	0	0	0	0	0
51	Influenzal meningitis	0	0	0	0	0	0	0
52	Influenzal meningitis	++++	++++	++	+	0	0	0

TABLE I—CONT'D

CASE	DIAGNOSIS	DILUTION OF CEREBROSPINAL FLUID						
		0	1:2	1:4	1:8	1:16	1:32	1:64
53	Influenzal meningitis	0	0	0	0	0	0	0
54	Influenzal meningitis	0	0	0	0	0	0	0
55	Influenzal meningitis	0	0	0	0	0	0	0
56	Influenzal meningitis	0	0	0	0	0	0	0
57	Influenzal meningitis	0	0	0	0	0	0	0
58	Influenzal meningitis	0	0	0	0	0	0	0
59	Influenzal meningitis	0	0	0	0	0	0	0
60	Influenzal meningitis	0	0	0	0	0	0	0
61	Influenzal meningitis	0	0	0	0	0	0	0
62	Influenzal meningitis	0	0	0	0	0	0	0
63	Influenzal meningitis	0	0	0	0	0	0	0
64	Influenzal meningitis	0	0	0	0	0	0	0
65	Influenzal meningitis	0	0	0	0	0	0	0
66	Influenzal meningitis	0	0	0	0	0	0	0
67	Influenzal meningitis	0	0	0	0	0	0	0
68	Influenzal meningitis	0	0	0	0	0	0	0
69	Influenzal meningitis	0	0	0	0	0	0	0
70	Influenzal meningitis	0	0	0	0	0	0	0
71	Influenzal meningitis	0	0	0	0	0	0	0

++++ indicates complete hemolysis.
+++indicates seventy-five per cent of cells hemolyzed.
++ indicates fifty per cent of cells hemolyzed.
+ indicates twenty-five per cent of cells hemolyzed.
0 indicates no hemolysis.

dilutions in these tubes were 1:2, 1:4, 1:8, 1:16, 1:32, and 1:64. Then 0.25 c.c. of a 5 per cent suspension of sensitized sheep cells was added to each tube. The tubes were shaken and incubated for one hour in the water-bath at 37.5° C. Following incubation they were allowed to stand at room temperature an additional two hours to permit the unhemolyzed cells to be deposited to the bottom of the tubes. Readings of hemolysis were then made; four-plus indicating complete hemolysis, two-plus indicating about 50 per cent hemolysis, etc.

One unit of complement would hemolyze 0.25 c.c. of sensitized cells* in these tests, according to the Hinton[11] technic for the Wassermann reaction. The results of these observations are recorded in Table I.

An analysis of these observations concerning the presence of hemolytic complement in the cerebrospinal fluid indicates that there is considerable variation in its presence. In most acute inflammatory conditions of the central nervous system it may be present in the cerebrospinal fluid in some cases. It is impossible to state just what factors are responsible for its appearance in some cases and not in others, even though the same etiologic agent may be operative. The degree of cellular response in the cerebrospinal fluid seems to bear no relationship to the presence of complement. In this series of cases complement was present more frequently in tuberculous meningitis than in the various types of purulent meningitis. The cellular response is, of course, much

*All suspensions of sensitized cells used in this study were very kindly provided by Dr. William A. Hinton's laboratory. The writer wishes to express his appreciation for this service.

less in tuberculous meningitis. Of great interest to us, at least, is the fact that complement was present much less frequently (in only five of thirty-six cases) in meningitis due to *B. influenzae*. It is probable that those factors which may considerably alter the permeability of the meningovascular barrier are responsible for the presence or absence of complement in the cerebrospinal fluid.

The hemolysis of sensitized cells which occurred in the cerebrospinal fluid of patients with hemolytic streptococcus meningitis is not necessarily due to complement. It is probably due, in most part, to streptococcus hemolysin in such spinal fluids.

DISCUSSION

The ultimate therapeutic value of complement in the treatment of meningitis still is an unsettled problem. Likewise, the exact mechanism whereby complement is operative in the serum destruction of those organisms causing meningitis is not entirely clear in all its details. It would seem most profitable to discuss these questions separately for meningococcus and *B. influenzae* meningitis.

Meningococcus Meningitis

With regard to the biologic destruction of meningococci two immune mechanisms may operate: first, there may be simply a complemental bacteriolysis of the organisms; second, there may be a phagocytic ingestion and destruction of sensitized organisms with or without the activity of complement. It is quite probable that this latter mechanism is the more important.

Davis[1] showed that normal human serum was distinctly bactericidal for the meningococcus. This property was diminished but not entirely destroyed by heating the serum to 60° C. for thirty minutes. Furthermore, meningococci were taken up by human leucocytes in the presence of human serum.

M'Kenzie and Martin[2] studied the bactericidal effect of human serums on meningococci. They found that the serum of normal individuals, patients with acute and chronic meningitis, and patients who had recovered had some bactericidal effect. It was much greater in patients who had recovered. The bacteriolytic action depended on a thermostable immune body which required the presence of thermolabile complement to complete the process. These authors made no observations on phagocytosis.

Kolmer, Toyama, and Matsunami[3] studied the opsonic activity of antimeningococcus serum in combination with normal serum. Normal serum or complement increased the opsonic activity of commercial antimeningococcus serum. For this reason these authors recommended the addition of 1 c.c. of fresh sterile human or guinea pig serum to each 9 c.c. of antimeningococcus serum.

In a subsequent paper Matsunami and Kolmer[12] found the bactericidal activity of horse antimeningococcus serum and normal human serum to be largely independent of complemental bacteriolysis. They found, however, that the addition of normal serum definitely increased opsonic activity and again suggested its therapeutic use. Evans[13] was unable to confirm the findings of Kolmer and his associates. She was unable to observe any reactivating effect when complement was added to commercial serum.

It is thus seen that the experimental evidence is incomplete regarding the rôle played by complement in the destruction of meningococci. Furthermore, practical therapeutic experience shows that many cases recover without the addition of complement to the antiserum. Indeed, on the basis of the observations recorded in this paper, the majority of patients do not have complement in their cerebrospinal fluid, yet the mortality has been reduced a great deal by serum therapy. We have had several patients who have made prompt recoveries in whom at no time during the course of the disease were we able to demonstrate complement in the cerebrospinal fluid.

On the other hand, an occasional patient, such as that of Bunim and Wies,[8] may be distinctly benefited by the addition of complement to the immune serum. The evidence is certainly insufficient, however, to recommend this as a routine procedure in the treatment of meningococcus meningitis. Nevertheless, if a patient fails to respond to a good specific serum and complement is absent from his cerebrospinal fluid, it would appear to be worth while to supply it.

In this connection it should be remembered that the blood of most normal adult individuals frequently has a considerable meningococcidal power. This has been shown by M'Kenzie and Martin,[2] Matsunami and Kolmer,[14] Matsunami[15] and Heist, S. Solis-Cohen, and M. Solis-Cohen.[16] Thus, human serum injected as complement may, in itself, contain specific immune bodies for the meningococcus.

If complement is used in treatment, the amount used probably should be much greater than that recommended by Kolmer and his associates. There are two reasons for this view: in the first place a small amount of complement would be tremendously diluted by the relatively large volume of cerebrospinal fluid into which it is injected; second, the Neisser-Wechsberg[17] inhibiting phenomenon* undoubtedly would play a rôle. Thjøtta,[18] in his study of this phenomenon, suggested that large amounts of complement may be necessary to overcome this inhibition.

In conclusion it would seem that the mechanism involved in the serum

*It was observed by these authors that when antiserum and complement were mixed in a bacteriolytic system, there was no killing of organisms in the greater concentrations of antiserum. Killing occurred only when the concentration of antibody was reduced markedly in relation to the amount of complement used. These observations which constitute this phenomenon have been abundantly repeated and confirmed.

destruction of meningococci should be restudied, particularly in respect to the newer knowledge of the antigenic structure[19, 20, 21, 22, 23, 24, 25] of the meningococcus.

B. Influenzae Meningitis

The serum destruction of influenza bacilli has been studied particularly by Ward and Wright.[5, 26] These authors have presented considerable experimental evidence that in the test tube the important killing mechanism is a complemental bacteriolysis, phagocytosis playing a very minor rôle. In test tube bactericidal experiments the following results were observed:

A. Inactivated immune serum plus organisms resulted in practically no bactericidal action.

B. Inactivated immune serum plus organisms plus fresh normal serum resulted in good bactericidal action.

C. Inactivated immune serum plus organisms plus washed defibrinated blood cells resulted in very little bactericidal action.

In these experiments the Neisser-Wechsberg[17] phenomenon was observed depending on the concentration of immune serum in relation to the amount of complement.

These authors have also shown that in addition to complement the thermostable immune body must be capable of precipitating the specific soluble substance of virulent influenza bacilli in order to be effective. Such an immune body results from a long period of immunization with a "smooth" or virulent antigen.

Since the important killing mechanism, in test tube experiments, is complemental bacteriolysis and since complement is so rarely present in the cerebrospinal fluid of patients with *B. influenzae* meningitis, the addition of complement to immune serum would appear to be definitely indicated in the therapy of this disease.

CONCLUSIONS

It has been found that complement is present in the cerebrospinal fluid in a small minority of patients with various types of acute inflammatory disease of the central nervous system. It is found only rarely in the cerebrospinal fluid of patients with *B. influenzae* meningitis.

A discussion of the use of complement in the serum therapy of meningitis is presented.

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GANGRENE OF THE FOOT FOLLOWING MEASLES

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GANGRENE, even including canerum oris, following measles is rare. Morse[1] does not mention gangrene at all other than noma. Kerley[2] does not mention gangrene at all, even noma. Holt[3] describes noma and says, "Gangrenous inflammations of other parts of the body are sometimes seen after measles, especially of the ear, the vulva, or the prepuce." Griffith,[4] citing Leitz, says that thrombosis of the vessels may result in gangrene of the limbs in exceptional cases. Abt[5] refers to the occasional occurrence of noma on other parts of the body, especially the genitals. Hoyne[6] reports cases of scarlet fever, measles, mumps, chickenpox, and whooping cough, occurring in the same individual in a period of forty-six days followed by an acute symmetrical dry gangrene, which he diagnosed Raynaud's disease. Recently Dick et al. reported a case of severe purpura with gangrene of the lower extremity following scarlet fever; and in June, 1934, the occurrence of massive skin gangrene complicating chickenpox was reported by Watson.[8]

On account of the dearth of information to be had from a perusal of standard pediatric textbooks and periodicals, one is forced to turn to treatises on dermatology for enlightenment concerning gangrene following the exanthemas. Schamberg[9] mentions the rare occurrence of gangrene on various portions of the cutaneous surface, other than the cheeks and genitals, citing Thomas, of Paris, Mayr, Faye, Battersaye, and Carroll, who have seen such cases. Sutton[10] states that dermatitis gangrenosa infantum, a rare disorder complicating varicella and vaccinia in certain cases, may more rarely follow measles and cites an instance reported by Thorp in *Lancet* in 1921. Andrews[11] published a photograph, by courtesy, of gangrene of the left knee and foot in that section of his text devoted to this condition. Whether this followed one of the exanthemas or developed independently was not mentioned.

CASE REPORT

Baby E. T., Jr., was fourth child of a tenant farmer who raised cotton and tobacco principally, some corn, and not enough hogs were raised to furnish the family with meat. He does not own a cow; the chickens are raised so haphazardly that there are no surplus eggs and chicken as a meat is not customary. The vegetable garden is merely a side issue and, because of the urgency of the call to the tobacco field, receives scant attention.

The baby, born normally at term, was breast fed with no regularity until after admission into the hospital. He had occasional attacks of colic as an infant; whooping cough which was said to be very severe at three months, and the mother says

that even now he loses his breath at times upon coughing. Since birth he has had constipation, for which the mother has been in the habit of giving castor oil. He sat alone at about the sixth month. Though he has had an occasional orange in his hand to eat of, he has not been given orange or tomato juice or cod liver oil. Since he was about six months old, he has been given crackers or pieces of biscuit. For the past several months he has had fried meat skins and chicken bone to chew on. He has had some candy but no vegetables. The first dose of diphtheria toxoid was given five weeks before admission; the other dose was not given because of the child's illness. He has not walked alone, but before the attack of measles he could walk around a chair, using both legs equally well.

On January 28 the appearance of a rash, which proved to be measles, was noted. The mother said the rash had disappeared by the end of a week. Following this, it was thought the child showed satisfactory improvement until February 10, when the child cried as if in pain. The parents were unable to discover any cause. The child appeared normally active and played throughout the next day, but the mother discovered two ulcers on the right foot that evening when she undressed him for bed. When questioned, the mother said she had seen no sign of anything wrong with the foot prior to this time. The child was seen by his local physician and referred to Park View Hospital, where he was admitted Feb. 13, 1934.

Fig. 1.

Fig. 2.

Physical examination was negative except for the following: Patient was flabby, anemic-appearing, white male infant with temperature 102° F. A slight nasal mucoid discharge was present, and there was some ulceration of the left naris. The lymph glands of the anterior cervical chain were palpable. There was slight beading at the costochondral junctions and some flaring of the costal angles with Harrison's groove. Crepitant râles were heard posteriorly over both lungs. The abdomen was moderately distended, and of the abdominal viscera only the spleen was palpable. The right foot was moderately swollen and presented two punched-out ulcers. One, on the dorsum extending in toward the inner malleoleus, was roughly triangular in shape, about 5 by 4 by 4 cm. in size. The other, roughly pentagonal in shape, surrounded the outer malleoleus and measured about 5 by 3½ cm. at the broadest diameter.

The laboratory findings were as follows: R.B.C., 4,810,000; hemoglobin, 55 per cent (Tallqvist); W.B.C., 24,000; polymorphonuclears, 30 per cent; lymphocytes, 70 per cent. A slight achromia was noticed; blood Wassermann reaction was negative. The blood culture was negative up to six days; urine examined at weekly intervals was negative except for an occasional pus cell.

For the first three days of his stay in the hospital, amertan was applied to the ulcers; after that only dry sterile dressings were used. A frame was placed over the crib, covered with sheets, and dry heat was furnished by electric light bulbs.

The ulcers appeared very painful for the first four or five days, requiring the administration of some Dover's powder. Cooked cereals were given twice daily. Vegetable soup or vegetable purées were given daily. The baby was weaned as quickly as possible. We met with considerable opposition from the mother on this point. However, the baby appeared to take lactic acid milk greedily. Mead's yeast, one teaspoonful in one-half ounce of orange juice, was given every four hours; thirty drops of cod liver oil were given in each feeding (every four hours). Prunes were given twice daily. Beginning the second day of his stay in the hospital, ultraviolet ray treatments were given daily in gradually increasing dosage, just short of marked erythema. The ulcer sloughed, but we thought healing took place with remarkable rapidity. The temperature ranged above 101° F., the peak being 103.4° F., with short remissions until March 3. For about five days before discharge on March 14, it had ranged within one-half degree of normal. The baby was taking food well and appeared to be generally quite improved when discharged from the hospital, although the ulcers had not completely healed over at that time. We have seen him three times since, the last time on Aug. 20, 1934, when photographs of the healed lesions were taken.

SUMMARY

1. An instance of gangrenous ulcerations of the foot following measles is reported.

2. From an analysis of the history one is forced to the conclusion that a nutritional deficiency existed. This probably predisposed the ulceration. "Measles may also aggravate a previously existing pathologic state, as tuberculosis, diabetes, heart disease, or other debility."[12]

3. On a balanced diet rich in vitamins and with the application of dry heat and ultraviolet ray, the child recovered satisfactorily.

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ACRODYNIA

Its Possible Cause

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THE literature of acrodynia is so voluminous and the clinical descriptions of the disease so complete that we will not attempt to review them or comment upon them beyond stating that since the disease was first described *arsenic* has always been under suspicion as *a* causative factor, though it has never been shown to be *the* causative factor.

The following case is reported, through the courtesy of Dr. F. L. Day, for three reasons: first, because we were able to discover the presence of a toxic agent in the patient; second, because we were able to determine the source of that agent; and third, for the purpose of stimulating investigation along the lines of our reasoning.

CASE REPORT

F. M., aged two years, male, was admitted to the Bridgeport Hospital May 13, 1934, on the pediatric service of Dr. F. L. Day. Past history was negative. The child developed normally and had always been well fed.

Family History.—Father and mother were both living and well. One other child was living and well. There was no known exposure to tuberculosis.

History.—The present illness began two months before admission when the patient had a severe attack of vomiting which lasted two days and was accompanied by some diarrhea. Within a short time he became irritable, lost his appetite, and gradually lost strength and weight. The bowels were inclined to be loose. An irritation developed on the buttocks and lower abdomen over the diaper area, but no rash or discoloration of the skin was noted elsewhere.

These symptoms persisted for a month (April 16) when the child was admitted to another hospital. While there he ran a slight fever ranging from 100° to 101.5° F., developed a mild cough and had mucous râles in both lungs. It was noticed that he perspired profusely. X-ray examination of the lungs and the Mantoux test were negative for tuberculosis. Stools examined for parasites were negative. The spinal fluid was normal. No skin findings were noted except on buttocks and lower abdomen.

The child was removed from the hospital after a stay of two weeks and a week later was admitted to this hospital.

Physical Examination.—The patient showed loss of weight and flabby musculature with sensitiveness of muscles on examination. He had no desire to stand or walk and was perspiring profusely. Some tremor of hands was noted. There was some irritability on examination, though not marked.

Head: Hair was thick, not falling out. Eyes and ears were negative. Nose: There was no discharge, no redness of the skin. The throat was somewhat reddened with large, ragged tonsils. The teeth were good. Mouth showed mild stomatitis.

In the lungs coarse, moist râles were heard over both sides. The heart was negative. The abdomen was scaphoid. No pain was elicited on pressure except in the muscles. The liver and spleen were apparently normal in size. No masses were felt. There was general redness over lower half of abdomen with marked papules irritated by scratching. Buttocks showed eruption of intertrigo type. Rectum was prolapsed about half an inch.

Extremities were clear except for distinct pinkish blush over all phalanges of fingers and toes and backs of hands and feet extending to wrists and ankles. Motion of these parts caused pain. Toes and fingers felt cold. There was marked itching of the hands, and especially of the feet. The child rubbed his feet together to relieve it. No desquamation was noted.

The day after admission one of us (C. V. C.) wrote: "Not acutely ill appearing, but pale and rather poorly nourished. Shows dry, pinkish, chronic-looking, slightly scaling, fine papular eruption over entire abdomen and a considerable amount on back. Hands and feet are somewhat pinkish and look as though chronically irritated. Some of the finger nails look abnormal. Fingers and toes seem a little hypersensitive. Baby appears to have some nervous system disturbance, showing a little tendency to tremor and rather slow and prominent respiratory movements. Lungs show râles of varying size and type. Rather large, slightly congested tonsils. Otherwise not remarkable. Acrodynia. Tuberculosis?"

A few days after admission pustules appeared around the toe and finger nails and on the sides of the fingers and toes. These became ulcerated and desquamation began. After two weeks the child developed furuncles on the back, buttocks, and in the palm of the left hand; these cleared up without complications.

Convalescence was uneventful, except for an attack of chickenpox, and (September 1) the patient was apparently well. He still perspired freely, and there was some thickening of the skin of the hands. Otherwise he seemed quite normal.

Laboratory Findings.—May 14: Hemoglobin, 93 (Sahli); R.B.C., 5,640,000; W.B.C., 7,250; polymorphonuclears, 49 per cent (Band 15); small lymphocytes, 39 per cent; mononuclear cells, 11 per cent; eosinophiles, 1 per cent. Blood appeared dehydrated.

May 15: Nose and throat cultures were negative for K. L. In the sputum smear acid-fast bacilli were not found. Widal test: Serum (1:40) did not agglutinate either of two strains of *B. typhosus*, or *B. paratyphosus* A or B.

May 26: Wassermann and Kahn tests were negative.

June 12: Organism from abscess was *Staphylococcus aureus*.

June 22: Hemoglobin, 77 (Sahli); R.B.C., 5,040,000; W.B.C., 8,950; polymorphonuclears, 55 per cent (Band 11); small lymphocytes, 27 per cent; mononuclears, 15 per cent; eosinophiles, 2 per cent. Red cells were slightly small and hypochromic.

August 28: Hemoglobin, 83 (Sahli); R.B.C., 4,450,000; W.B.C., 10,600; polymorphonuclears, 47 per cent (Band 2); small lymphocytes, 37 per cent; mononuclears, 3 per cent; large lymphocytes, 8 per cent; eosinophiles, 4 per cent.

X-ray Examinations.—May 14: A radiographic examination of the chest showed no evidence of infiltration in either peripheral lung field. Although the hilum shadows were moderately thickened, there was no evidence of calcification to suggest childhood pulmonary tuberculosis.

June 23: A radiographic examination of the bones of the knees, the forearms, and the wrists showed no evidence of gross pathology. There was a slight increase in the calcification at the distal diaphyseal ends of the shafts, especially in the wrists. There was no evidence of plumbism. The epiphyseal development appeared normal.

Having in mind the case reported by Meyer and Weise[1] in which arsenic in large amounts was discovered in the blood and urine, we investigated the diet to discover, if possible, a source of arsenic. The most likely source seemed to be the home-grown, home-canned string beans which had been heavily sprayed with arsenate of lead by the patient's father and which had been a regular article of diet, both fresh and canned. Accordingly, several cans of these beans, together with samples of the patient's hair, blood, and urine were forwarded to Dr. C. N. Meyers, to whom we are indebted for all of the analyses included in this report. These samples were collected twelve days after admission and showed the following amounts of lead and arsenic:

Beans, sample 1—	0.34	mg. arsenic per 100 gm. of solid
Beans, sample 2—	0.083	mg. arsenic per 100 gm. of solid
Beans, sample 3—	0.29	mg. arsenic per 100 gm. of solid
Bean juice—	0.259	mg. arsenic per 100 gm. of solid
Hair—	0.078	mg. arsenic per 100 gm. of solid
Urine—	0.24	mg. arsenic per 100 gm. of solid

Beans, sample 1—	4.3	mg. lead per 100 gm. of solid
Juice, sample 1—	9.5	mg. lead per 100 gm. of solid
Juice, sample 2—	10.4	mg. lead per 100 gm. of solid

Unfortunately, the amount of blood submitted was insufficient.

These figures are high. The amount of arsenic in the hair is greater than that found in the hair of a person who was suffering from the symptoms of arsenic poisoning,[2] and the same is true of the amount found in the urine.[2]

On the other hand, a sample of urine collected twelve weeks after admission showed 0.059 mg. arsenic per 100 gm. of solid and 0.026 mg. of lead per liter. A sample of blood collected at the same time showed a trace of arsenic and of *lead* 0.98 mg. per 100 gm. of solid (normal 0.05 mg.).

Three theories are most commonly advanced as to the cause of acrodynia: first, that the condition is an infectious one; second, that it is an avitaminosis; and third, that it is due to dysfunction of the vegetative nervous system. To these we would like to add a fourth, or perhaps amend the third—that is, that acrodynia is the result of metallic poisoning acting on the vegetative nervous system in peculiarly susceptible individuals. In our opinion the metals causing this poisoning may be arsenic and lead *in combination*, such as is found in the widely used insecticide *arsenate of lead*.

Some of our reasons for this theory are as follows:

Before the use of insecticides this disease was unknown. With the increase in their use the disease has become more prevalent.

The results of treatment point to the fact that the disease is due to the ingestion of some toxic material. Various treatments have been advocated, ranging all the way from removal of the tonsils to special diets. They all seem to have been successful. They all have one thing

in common. That one thing is a change in diet. In almost every instance this change in diet has been brought about by removing the patient to a hospital.

Considered from this point of view much evidence in the case reports is corroborative. In reporting a group fed with liver, the author[3] says of one case, "This case is interesting because an attempt was made to give the liver treatment at home—the treatment had apparently completely failed—and the child was admitted to the hospital for further trial," with success. Here the diet was certainly changed by removing the patient to a hospital, and apparently no improvement was noted until the change in diet.

In a series reported by another author[4] we read, "The patient was admitted in September, 1929, and after eleven weeks was discharged (at the parents' request) improved, was readmitted in January, and died four weeks later." Here the diet was changed with resulting improvement which was undone, in our opinion, by a return to the original toxic diet.

That lead arsenate may be the toxic article in the diet is indicated in other reports. One writer[5] has it that "three weeks before admission the child ate a large quantity of canned cherries and had a severe attack of diarrhea." Analyses have shown the possibilities of arsenic and lead in this particular kind of canned fruit.[2] Again we read[4] of a child who "dwelt in poor circumstances on a farm, though the mother gave the child good care and nourishing food." (Our own patient dwelt on a farm, and his mother gave him good care and nourishing food. His diet was entirely adequate and well balanced.) Of another case the author states that "during the two months previous to admission the mother had difficulty in feeding the baby, who was accustomed to cow's milk and vegetable broths." Both of these cases strongly suggest arsenate of lead in the diet. Our own case showed it.

Apparently the length of time during which the toxic agent is ingested before a change in diet is made has a great deal to do with the ultimate outcome of the disease. A recent report[6] of an autopsied case states that the patient had been ill for approximately six months before admission to the hospital, during which time he had been treated at home. In another series[4] a case terminated fatally, which "began eleven months previous to admission" and another fatal case in the same series "showed evidence of long-standing illness." On the other hand, patients who had had symptoms for "eight weeks," "two months," "nine weeks," "four weeks," and "three months" previous to admission all recovered.

The autopsy findings in the nervous system are not at all incompatible with what we would expect to find in chronic lead poisoning. The similarity of the disease to chronic arsenic poisoning was noticed

long ago. We feel that this symptom-complex may very well be due to the action of arsenic and lead *in combination.*

In the case presented we know we had arsenic poisoning. We know we had lead poisoning as well. But the clinical picture was that of acrodynia.

Is acrodynia arsenoplumbism in peculiarly susceptible individuals?

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144 GOLDEN HILL STREET
881 LAFAYETTE STREET

AN IMPROVED CONTAINER FOR HYPODERMIC SYRINGE

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THE administration of a hypodermic injection in the doctor's office is a simple procedure. In the patient's home it is often a cumbersome and time-consuming operation because of the lack of adequate facilities for sterilizing syringes and needles. Yet in spite of the obvious disadvantages incident to boiling a syringe in a kitchen pot over the stove, most physicians prefer this to carrying a previously sterilized syringe in an inadequate container, particularly one which cannot itself be boiled. Such cases must be filled with some type of disinfectant fluid, none of which is as certain in its antiseptic action as boiling, and many of which may have a deleterious effect upon injectable biologic products.

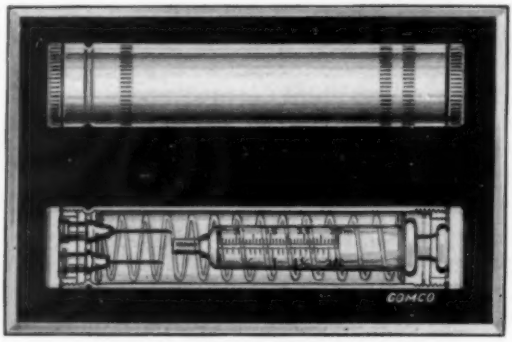

Fig. 1.

As a solution to this problem a case has been designed which will carry a dry syringe and maintain its sterility under all conditions. It is made entirely of rust-proof metal and is unbreakable. It will hold firmly a 2 c.c. syringe of any design and two hypodermic needles of any style or length. The syringe, needles, and case may be boiled together, and, when the two caps are then screwed in place, the contents are unquestionably and permanently sterile. The caps are water-tight and air-tight, and therefore, no matter how carelessly the case may be knocked about in the doctor's bag or what liquid may be spilled upon it, there is no possibility of contamination.

The outfit is made shockproof by means of pressure from a flexible coiled spring which prevents the contents from rattling about and thus

insures against dulling of the needle points and breakage. The same spring causes the syringe to protrude slightly when the cap is removed, thus facilitating its easy extraction from the case.

Because the case is impervious to chemical action of all liquid sterilizing mediums, these may be used when indicated (as for example by a diabetic patient on a journey during which several injections of insulin must be taken with no opportunity to boil the outfit between injections). An important feature of this set is the fact that sterilization may be attained by boiling the entire outfit, including the case. The absence of a blind bottom allows free circulation of the boiling water and promotes cleanliness. After boiling, the syringe need not be touched, and no fluid need be added.*

*This case is manufactured by The Gomco Surgical Manufacturing Corporation, Buffalo, N. Y.

Critical Review

GROWTH AND DEVELOPMENT

The Endocrine Glands and Growth

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THIS series of reviews on the subject of growth and development is attempting to present the subject first, from the standpoint of the nature of growth as a process, and second, from that of the various physiologic and biologic factors acting upon the process. It has been shown that general growth occurs in a series of waves, or curves, superimposed upon a more gradual increment in the development of each individual and that in the various separate organs and tissues in the body, differing growth rates prevail so that the summation is an orderly development in which nutritional and functional demands are met as they arise in the normal individual. The stimuli which give rise to these growth rates, both general and in specific tissues, are little understood, but some of the factors, such as the vitamins and hormones, are gradually emerging into the light of day. For the unknown factors we have to fall back upon such indefinite terms as organismic pattern or natural tendency.

It has been shown quite clearly that most of the vitamins exert a marked effect on general growth since deprivation of any one of them, except possibly vitamin E, results in complete cessation of growth. In addition to this influence upon the general growth impulse, all of them exert effects of specific nature on separate organs or tissues of the body as, that of vitamin A on epithelial structures, that of vitamin B on nervous tissues, that of vitamin C on the vascular system, etc. In this present consideration of the endocrine glands and their secretions as they affect growth, the situation is somewhat different. With the brilliant exception of the growth hormone of the anterior pituitary gland, their effects upon general growth are much less conspicuous, and their results upon specific structures are, if anything, more sharply defined.

It must be understood clearly that both vitamins and hormones probably act as specific catalyzers of general and local growth, influencing living protoplasm which is unfolding according to some underlying, less obvious control.

Our understanding of the respective rôles of the various endocrine glands in the general and specific growth problems is made more difficult by another factor not complicating our consideration of the vitamins. This is the fact that the various glands with their multiple hormones comprise a system interacting upon themselves to a degree and in a manner of which we are only partly aware. This has been and probably will continue to be a source of error in the appraisal of

the effects of separate hormones. However, it will probably be best to consider the glands separately, realizing that they seldom act as independent units.

Another fact seldom mentioned in the consideration of the relation of hormones to growth is the reactivity of the receptor tissues to these substances. Smith and Engle bring out the point that hormone effects depend upon the sum of endocrine stimulating power and the ability of the tissues to respond. Thus, it has long been known that, in making limb and organ transplants in amphibia and other lower animals, the ultimate size of the transplant is dependent upon the size of the donor rather than upon that of the recipient. No amount of endocrine stimulation has enabled investigators to enlarge transplanted tissues beyond the size of the species from which they originated. A differential growth rate is, therefore, present which is to a certain extent independent of hormones.

THE PITUITARY GLAND

Because the pituitary, or hypophysis, elaborates the general growth hormone and because we are beginning, at least, to understand some of the interrelationships between this gland and other endocrine structures, it affords a logical starting place in this discussion.

Historical

The hypophysis has been known to exist since the time of Galen, A.D. 200, when its function was supposed to be that of lubricating the throat. This idea held until about 1660, at which time it was overthrown by Schneider who considered the gland a vestigial structure. About 200 years later, in 1864, we see the first implication in the literature that the pituitary is of importance in growth. Verger reported the case of an acromegalic giant with an abnormal pituitary gland. Again, thirty years later, Klebs published a monograph on acromegaly and demonstrated abnormally large pituitary glands in his cases. Marie, in 1886, definitely established a relationship between this gland and acromegaly but considered the disease due to a deficiency. In 1871 Lorraine described pituitary dwarfs. Before this, in 1840, Mohr had reported a patient suffering from the condition we now recognize as pituitary adiposity, with hypophyseal tumor revealed at autopsy. But it was not until 1901 that Fröhlich described the syndrome which now bears his name, dystrophia adiposogenitalis. In 1895 Oliver and Schafer discovered a secretion recovered from the posterior lobe which was effective in raising the blood pressure. Cushing in 1912 published a monograph on pituitary tumors and their effects as well as his results in surgical treatment.

It was not until after 1920, however, that the isolation of the separate hormones took place. Evans described the growth hormone in 1921; Smith, the ovulating sex-stimulating hormone in 1926; and Zondek, the luteinizing hormone in 1928.

The foregoing brief sketch of the history of research in this subject omits the names of many who have contributed much to our knowledge and is not intended to be complete. Engelbach in his work, *Endocrine Medicine*, gives a detailed account for those historically inclined.

ANATOMY AND HISTOLOGY

It is necessary, before one can understand the pituitary function, to have clearly in mind the anatomy and histology of the gland, as well as its relationship to the neighboring brain. The organ is found in all vertebrates. Its origin can be noted in the human embryo as early as the fourth week, at which time the upward extending pouch from the oral cavity has made contact with the infundibulum descending from the brain. The epithelial portion, that from below, forms the anterior lobe; the neural portion gives rise to the posterior lobe. Between these two is the cleft, and along the cleft margin of the posterior lobe lies a thin envelope of epithelial tissue which develops into the pars intermedia. Along the infundibular stalk lies a similar sheet of cells forming the pars tuberalis.

It would at once seem likely, because of its twofold origin, epithelial and nervous, that the gland would not function as a simple secretory organ. One immediately thinks of the similarity between this arrangement and that found in the suprarenals with the glandular cortex and the medulla so intimately associated with the sympathetic nervous system. The products of the anterior lobe, with which we are here chiefly concerned, are probably taken up by its rich vascular supply and distributed to the body by this route. Those of the pars intermedia and pars tuberalis, however, are probably not disseminated in this manner because the blood supply is very poor and because the anatomic relationships indicate that they are either discharged into the brain cavity, or are stored in the posterior lobe and adjacent brain substance, and are slowly given up from these structures. Hoskins says: "Determination of the function of the pituitary as such is rendered difficult by uncertainty as to the precise relationships between the gland and the adjoining parts of the brain. Injuries of this region of the brain, hypothalamus, produced experimentally, by accident, or by the growth of tumors, have been shown to lead to such disturbances as obesity, excessive urine formation, and abnormalities of sugar metabolism. Very similar disorders are producible experimentally by injuries to the pituitary. There is some evidence, also, that from the brain tissue in the hypothalamic region can be obtained an active extract that shares in the properties of pituitary derivatives. A third paradoxical element in the situation is that severe injuries of the hypothalamic region may either produce the abnormalities just mentioned or may result in no detectable disturbance of function whatever. The answer to the riddle at this time can only be surmised. The known facts suggest that the pituitary and the hypothalamus stand in an intimate relationship somewhat similar to that of the adrenals and the sympathetic nervous system. It would appear to be true that the composite mechanism normally acts as a unit susceptible of disturbance in either of its parts with ultimately similar results, but that either the nervous or the glandular mechanism can substitute for the other. As specific evidence in favor of this latter supposition, the fact can be cited that profuse urinary output caused by injury to the hypothalamus can be readily controlled by administering an extract from the posterior lobe."

Since recent advances in our knowledge have enabled us to tell the exact hormones elaborated by some of the cell types, the histology of the hypophysis has become of primary importance. In the anterior

lobe there are three predominant types of cells; first, the alpha, acidophilic, or eosinophilic cells, known to secrete the growth hormone; second, the beta or basophilic cells, which probably secrete the sex-stimulating hormones; and third, the chromophobe, reserve, or chief cells, whose function is not finally established. These are all polygonal cells with granules and are named after the staining propensities of these granules. Some authors believe that the chromophobes are the parent cells of the other types, others that the chromophobes secrete the sex hormones, though this is doubtful. In the adult gland the eosinophilic cells comprise about 37 per cent, the basophilic about 11 per cent, and the chromophobes about 52 per cent of the cells. These relationships are not constant throughout life, however; much interesting work is being reported upon this subject.

In addition to these three types seen in normal glands, under two pathologic conditions other types are seen, pregnancy and castration cells. The cells of pregnancy occur in such large numbers as to cause gross enlargement of the gland at this time. After delivery they decrease but do not entirely disappear. The cells of castration appear after this operation together with an increase in the percentage of eosinophiles. This checks nicely with the well-known increase in stature of eunuchs operated upon before closure of the epiphyses. Castration cells are two or three times the size of the alpha and beta cells, and the protoplasm, which contains granules, stains pink.

The cells of the central portion of the posterior lobe are neuroglial except for a few epithelial cells which appear to have migrated from the pars intermedia. Since the blood supply of this structure is so poor, it is not considered that it has a secretory function. The fact that potent extracts may be prepared from it, however, indicates that it has a storage function for the hormones elaborated by the neighboring pars intermedia and pars tuberalis.

The pars intermedia, which also has a poor blood supply, is distinguished histologically by (1) cells resembling the chromophobes, (2) elongated cells which may be stained by the Golgi method, and (3) cysts containing colloid and hyaline material. It is thought that the cells of the pars intermedia secrete the posterior lobe extract which is merely stored in the pars nervosa before absorption into the circulation or brain cavity. It is also supposed that these cells secrete the hormones that dilate the melanophores of frogs and other animals.

In the pars tuberalis no granular cells are found, but the cells are arranged in columns about cavities with no epithelial lining. These cavities are not found until the fifth postnatal month. Squamous cells are also found extending out into the pars nervosa, to the floor of the fourth ventricle, and into its nervous tissue.

In the infantile period the two portions of the gland are not united entirely, and the intervening cleft is distended with colloid material. The anterior lobe is filled with small, pale appearing cells. Chromophobes are present in the first year. During the juvenile period there is marked increase in the size and number of the eosinophiles and development of the pars intermedia. At adolescence there is a marked increase in the basophiles and chromophobes which persists until the age of about forty. At this time there are relatively fewer eosinophiles, and the cleft progressively closes. In old age the cleft is com-

pletely closed uniting the gland into a compact mass. The epithelial cells diminish, connective tissue increases, and the gland becomes less vascular.

It is known that the hypophysis functions during fetal life because potent extracts have been made from pig embryos of half full size and because its removal, notably in tadpoles, has prevented subsequent normal development of structures known to be under pituitary control, thyroid and suprarenal glands.

This histologic résumé is given because it shows that the appearance of the gland cells under the microscope coincides roughly with the functional demands of different age periods. During the major growth epoch the acidophilic cells reach their greatest development, and during sexual maturation the basophiles reach their maximum percentage.

THE EXPERIMENTAL APPROACH

It is interesting to note the steps by which our knowledge of hypophyseal function has progressed. At first, on the basis of propinquity alone, it was assumed that the gland secreted a fluid into the throat. When this hypothesis, after centuries, was overthrown, the gland was thought to be merely vestigial. Then, as a result of careful autopsies, various observers established its relation to growth disorders: first to acromegaly, then to dwarfism, dystrophia adiposogenitalis, and gigantism. At about this time, when it became apparent that a gland of internal secretion was being dealth with, attention was shifted from the growth aspects of the problem by the discovery of the posterior lobe hormones which had no growth function.

It was not until the era of experiment upon lower animals that the growth factor again became of major importance. The effects of pituitary removal, destruction, transplantation, and feeding were studied in hundreds of experiments. These were at first crude and inconclusive because of surgical difficulties encountered and because of the fact that true pituitary effects were difficult to evaluate in animals with intact hypophyses. The ideal experiment was to remove the glands from animals, note the effects, and then to attempt replacement therapy with feeding, transplantation, or hormone injection. This line of investigation was given great impetus by a perfection of technic by Smith, who showed that in the rat complete removal transorally was possible without disturbing the brain. This obviated the secondary results known to follow injury to the hypothalamic region. Since this technic was discovered, evidence as to the exact influence of pituitary secretion on growth has rested upon unusually firm experimental ground. The growth- and sex-stimulating hormones have not only been demonstrated, but they have also been isolated.

Along with this experimental activity in the laboratories resulting in hundreds of articles and books, great interest has been displayed in the clinics explaining the pathogenesis of pituitary disturbances on the basis of endocrinologic advance and pointing out new hypophyseal syndromes such as basophilic adenoma, Cushing's disease, and pituitary cachexia, Simmond's disease. At the present time, since this topic is in its most active phase, one expects to find pituitary disclosures in almost any medical periodical. Whether we are on the verge of discoveries which will make us masters over general growth through

the growth hormone or give us control of maturation processes through the sex hormones is a matter for the near future to decide.

For many years a controversy raged as to whether or not pituitary hormones were necessary for the preservation of life. This issue was complicated by imperfections in the technic of operative removal and lack of sufficient long-time mortality statistics on the animals. According to Evans, it is now quite evident that removal of the hypophysis has no immediate serious effect upon life. He is equally sure, however, that "most hypophysectomized animals succumb from cachexia before anything like a normal life span has been passed."

THE GROWTH HORMONE

The isolation of this specific hormone was largely due to the work of Evans and his collaborators. It is known to be secreted by the acidophilic cells of the anterior lobe. As far as can be established, the growth hormone stimulates growth in every structure in the body. When the pituitary gland is removed from immature animals, the effect is immediately noticed in cessation of growth and development. As a corollary, growth can be reestablished in these same animals by administration of the growth hormone or by pituitary transplantation.

There seems to be no clear-cut statement of opinion in the material which has come to my attention as to the mechanism of this growth stimulation. However, Collip and his coworkers have this to say: "— a few facts which we believe are important in the understanding of the mechanism of the action of the growth hormone. We have observed that the compensatory hypertrophy of the remaining kidney occurs in hypophysectomized rats after unilateral nephrectomy; furthermore, Dr. Jeffers has found in his laboratory that mitotic figures are plentiful in the mammary glands of hypophysectomized rats at the time of parturition. It is also well known that the proliferation of epithelial cells and fibroblasts in wound healing is not seriously interfered with by hypophysectomy and that transplanted tumors grow, though not as rapidly as usual, in hypophysectomized rats. All of these observations show that the proliferation of cells and the growth of the individual organs are not necessarily dependent upon the growth hormone. That animals may survive hypophysectomy for several years shows distinctly that cells of the various organs that died during this period have been replaced by new ones. The present paper shows that even a general growth, though not increase in length, of the osseous system may be produced in the absence of the pituitary growth hormone.

"We conclude that the growth of the various organs in themselves is largely independent of the hypophysis. Apparently the function of the pituitary growth hormone is only to permit enlargement of the size of the body as a whole, with a harmonious and proportional increase in the size of all the organs."

It would be interesting to learn what effect, if any, this hormone would have on tissue cultures. It seems to me that the statement quoted above might imply that maintenance cell division could proceed without the growth hormone but that general growth and development under specific organismic patterns is stimulated by this substance.

While removal of the hormone causes a cessation of growth and a condition of status quo, Evans remarks that "this is not the establishment of a perpetual youth, for the capacity of the body in many measurable ways has been injured." In dwarfs, for instance, he states that there is actual shrinkage of the epiphyseal cartilages and gradual obliteration by dentin of the pulp cavities of the incisors, together with marked disturbance of the calcium metabolism and reduction of the blood calcium. This last may possibly be due to secondary parathyroid insufficiency. The failure of the bones to increase in length is apparently due to lack of the formation of cartilage in the epiphyseal discs.

Not only has the growth hormone restored growth in hypophysectomized animals, but also gigantism has been experimentally produced. These growth effects have been most perfectly attained with the preparation of Evans. Reichert warns that the sex-stimulating hormones must be completely removed in such solutions because they tend to close the epiphyses and stop growth. It is noted that there is a decided sexual difference in response to this hormone, the males reacting less promptly to administration and withdrawal of the hormone.

Most laboratories use rats in the test for the presence of the growth hormone because in this and similar species the epiphyses remain open during adult life. As a result, it is possible to measure the stimulus to body growth after maturity. In practice, the test applied is to use animals between five and nine months old which have reached a stage of development called the "growth plateau," in which their slight weekly increment is known by previous observations. Intraperitoneal administration of potent extracts will produce marked accelerations.

In experimental animals the growth of which is being stimulated by the hormone, more protein is stored and less consumed than normally. This effect is comparable to that of insulin in the sugar metabolism.

In answer to the question as to the purity of the preparations produced, Evans states: "It is easy to produce a white hygroscopic powder, stable for months at room temperature in dry, air-exhausted chambers and capable of producing maximum results in adult female rats in doses of considerably less than 0.5 mg. daily. The powders have almost 15 per cent of nitrogen, all in the form of protein or a protein-like body, and it is difficult to break this down further without losing efficiency. It appears that just as they are proving helpful in the isolation of enzymes, selective absorption methods will be of great importance here."

In the earliest stages of development, growth seems to proceed without the activation of this hormone. In amphibia the pituitary has been removed before structural differentiation was demonstrable in the gland. Such larvae develop to the tadpole stage at a rate only slightly retarded, after which they show the effects of hormone deficiency unless administration is artificially afforded. Secondary failure of the thyroid to develop is a contributory cause for this lack of development for partial compensation is seen when the thyroid hormone is given such animals.

Considerable skeletal growth takes place in the rat when the pituitary is removed even as late as the weaning period. Later in life, however, growth is immediately stopped by hypophysectomy. Difficulties in technic have prevented investigators from discovering whether or not removal of the gland at birth would stop growth, but

from the observation above it is thought that some growth would take place under these conditions. This is one of the reasons why most investigators doubt that congenital growth disturbances such as achondroplasia are due to endocrine factors.

One of the most interesting pituitary growth anomalies I have seen referred to is noted by Smith and Engle, that of hereditary dwarfism in a strain of mice. In this strain, dwarfism occurs in the mendelian ratio, and the dwarfs are sterile. In the offspring of the heterozygous, apparently normal animals, growth proceeds as usual for about fifteen days, after which it may rather abruptly slow down and finally stop entirely. The pituitary glands of these dwarfs are undersized and histologically show complete absence of acidophilic cells.

THE GONADOTROPIC HORMONES

Although these hormones do not directly influence general growth, they produce marked effects on specific growth of the organs concerned with reproduction. There are two, and possibly three, such hormones: that which stimulates the ovulation function, one which increases luteinization, and possibly one which fortifies the pregnancy urine hormone. Understanding of the gonad-stimulating hormones is complicated by the fact that the sex glands themselves secrete hormones and by the fact that additional endocrine products in pregnancy and castrate urine have gonadotropic effects. For these reasons it is necessary to define these various substances and give their sources as far as is known.

The female sex hormones are estrin and progestrin, both secreted in the ovary. The first functions in promoting estrus and in the development of the secondary sex characteristics, the second, in the processes of pregnancy, luteinization, etc. Their production is stimulated by the pituitary gonadotropic hormones, and in turn the sex gland hormones inhibit the production of those from the pituitary.

The pregnancy urine hormone, prolan or theelin, causes stimulation of the corpora lutea and probably originates in the placenta, according to Smith. It is often spoken of as a pituitary hormone, an error partly due to the different nomenclatures used in various countries. In male animals this substance stimulates the secretion of the interstitial cells of the testes and consequently hastens development of secondary sex characteristics. Engle and others have used it to promote descent of the testes in cryptorchism. Of course, it is not of interest in the male from a physiologic standpoint because males are not under normal conditions exposed to its effects.

The castrate urine hormone, on the other hand, acts upon the follicles of the ovary in females and upon the tubules of the male, according to Smith. It is considered by many authors that this is a true pituitary hormone, but absolute proof is lacking.

It is established beyond doubt that in all young experimental animals, as well as in human beings, removal of or destruction of the pituitary results in lack of development of the sexual system. In mature animals the same lesions cause regression of the system. Sex interest is lacking in such animals. The germ cells, ova and sperms, however, remain alive in the tissues, and subsequent administration of pituitary hormones is capable of complete restoration of sex function. In young rats the stimulating effects of pituitary transplants on the

sexual system are evident almost immediately, in two or three days, the females responding more rapidly than the males. This sexual hypertrophy or premature development, however, is anatomic rather than physiologic because functional maturity does not occur until the adolescent age in the various species.

Evans devotes considerable space to a discussion of a fraction of the pituitary secretion which interacts with prolan to form the most potent sex-stimulating substance known. He and other authors consider that these two substances activate each other because neither one alone is as potent as are the two combined. Of the two, the pituitary fraction is by far the most potent. This prolan-stimulating substance is different from the two well-known gonadotropic hormones of the pituitary. Separate preparation of the gonad-stimulating hormones is being attempted but has not been accomplished.

Since the true sex gland hormones inhibit the production of those from the hypophysis, several investigators have referred to their interaction as the cause for the female sex rhythm. To quote Hoskins, "when the pituitary activity is at its height, it is assumed that this leads to the induction of a new sex cycle. The augmented supply of gonad hormones then leads to the unfolding of the sequential development in the sex organs and at the same time induces a quiescent period in the pituitary. The sex hormones having waned, the pituitary resumes activity and a new cycle is begun. Such observations quite justify the designation recently conferred upon the anterior pituitary, 'the motor of the gonads.' "

THE LACTOGENIC HORMONE

Work by Riddle and Corner and others makes it seem probable that the anterior pituitary secretes a hormone capable of stimulating mammary glands. This hormone, prolactin, is apparently potent only on mammary glands prepared by the sex hormones. Under its influence virgins and even male animals have been made to produce milk. This hormone may be of great importance to pediatrists if it is prepared in a form practicable for use in human beings. The writer feels, however, that even with a potent lactogogue in our hands there would still be plenty of mothers who would not be able to nurse their babies.

THE THYROTROPIC HORMONE

Evidence as to the existence of this hormone rests upon the established fact that removal of the pituitary gland results in reduction in the size of the thyroid gland and in changes in the epithelium which lead to the formation of squamous cells with flattened nuclei. The substance has not yet been isolated in pure form.

Hypophysectomy results in a lower basal metabolic rate than that produced by thyroidectomy. This is probably due to the fact that hypophysectomy also affects the suprarenal glands, which exert an influence on basal metabolism. In experimental animals exophthalmos has been produced by administration of the pituitary thyroid-stimulating substance. This is explained on the basis of superstimulation of the thyroid.

THE ADRENALOTROPIC HORMONE

When the hypophysis is completely removed from experimental animals, in addition to the changes previously mentioned, there is an almost complete atrophy of the adrenal cortex. It has been thought

that the gradual decline in vigor and health that the animals showed might be due to the lack of cortin. On the other hand, in such animals, whereas the administration of cortin did not improve their condition, aqueous alkaline extracts of the anterior pituitary caused an immediate favorable response. The substance in the anterior pituitary responsible for this change is apparently closely allied to the growth hormone, not to the gonadotropic fraction. It has been assumed that under normal physiologic conditions this pituitary secretion activated cortin. It may be that in the future a pituitary hormone may be used either alone or in conjunction with cortin in the treatment of Addison's disease.

THE PARATHYROID-STIMULATING HORMONE

Evidence suggests that there is a pituitary substance which stimulates parathyroid activity, but this is as yet inconclusive.

THE PITUITARY AND OBESITY

Since operative technics which did not disturb the neighboring brain have been used, adiposity as a result of hypophysectomy has become a rare observation. Pituitary dwarfism produced under the best modern technics is not associated with adiposity. Consequently the concept that the syndrome of Fröhlich was due to lack of pituitary hormones has been losing ground. It is being more and more generally thought that this is a disturbance on a nervous basis, due to hypothalamic dysfunction.

On the other hand, Anselmino and Hoffman have isolated a substance from the anterior lobe which when injected into animals increases the acetone bodies in the blood. Under normal conditions this substance is found in the blood only when fat is being burned and would seem to tie the pituitary with fat metabolism. That Cushing's disease, pituitary basophilism, is characterized by adiposity of the face, neck, and trunk, raises the question as to whether the hypophysis can be disregarded in this connection. It is, of course, conceded that pituitary tumors cause adiposity by pressure effects on contiguous areas in the brain. Probably the central and autonomic nervous systems are quite as potent factors in adiposity as are the hormones.

THE DIABETICOGENIC HORMONE

Since this hypothetical hormone has no direct effect on growth and development, it is mentioned for the sake of completeness only. It is likely that diabetes of pituitary origin is a clinical entity.

THE RELATIONSHIPS OF THE GROWTH AND GONADOTROPIC HORMONES

It is apparent from the results of animal experimentation and also from a few clinical facts that the growth and sex hormones of the hypophysis are mutually inhibitory. When the sex hormones are included in the material injected into rats to produce growth, for instance, much less increment is obtained than is the case when the growth hormone is given alone. Also, it is a well-known fact that in acromegaly, a disease due primarily to increased production of the growth hormone, marked decrease, or absence of sex activity is noted.

It is interesting that in this small gland, then, are lodged the determiners of youth and maturity. As long as the activity of the acid-

ophilic cells and the consequent production of the growth hormone predominates, general growth and particularly that of the epiphyses proceeds. But with the increase in function of the basophilic and chromophobic cells in the pituitary and the resulting rise in production of gonadotropic hormones, maturation takes place rapidly, and with this process the epiphyses close and growth ceases. This cessation of growth is absolute in higher animals but may persist in much modified degree in some lower forms such as the rodents.

Not only are the pituitary gonadotropic hormones antagonistic to growth, but also the true sex hormones elaborated in the sex glands share in this property. This probably accounts for the phenomenon of eunuchoid gigantism. In the absence of sex hormone inhibition the growth hormone continues its influence on the organism, producing great stature.

THE POSTERIOR LOBE HORMONES

So far, the secretions of the anterior lobe only have been discussed. It is almost certain that the pars nervosa has no secretory function although, as is well known, extremely potent hormones may be extracted from this tissue. It is more probable that the hormones that cause increased smooth muscular contraction and decrease the urinary output are elaborated by the pars intermedialis and pars tuberalis and excreted into the pars nervosa and around the infundibular stalk into the brain cavity, thus accounting for the hormonic activity of extracts from this region. It is possible that a fat metabolic agent may also be elaborated and secreted in this manner.

Since none of these hormones are directly concerned with the growth problem, it is proper to dismiss this subject with this brief statement rather than to discuss the voluminous arguments and evidence.

CLINICAL IMPLICATIONS FOR THE PEDIATRIST

Any structure so vitally influencing growth must be of absorbing interest to physicians limiting their work to patients in the growing period. Just how far we are justified in assuming that laboratory results obtained on lower animals, or even on primates, are applicable to human beings is an open question. While we certainly cannot apply all of them at face value, some of the facts seem so uniformly true in all species that it is justifiable to assume, until the contrary is proved, that they apply to human beings.

Dwarfism of the pituitary type, in which there is no bodily disproportion, may command our close attention from the standpoint of therapy in the near future. Such dwarfs vary greatly in their appearance and functional capacity according to the time of onset and the severity of the pituitary deficiency. They vary also depending on whether the growth function alone, or that plus the gonadotropic function is impaired, resulting in such individuals in many states of physical and sexual development. Their mentality is not, as a rule, affected except so far as their psychic make-up is changed by the fact that they are more or less freaks to the rest of mankind. In addition to the infantile proportions, receding chin, flat chest, protruberant abdomen, low umbilicus, and delicate skin, it is found that the epiphyses do not close. Some of these men and women have lived to very old age and were quite famous characters in history. If they mature sexually, they may propagate and their children usually grow to normal stature.

Engelbach has reported the successful administration of the growth hormone to such a patient, a nine-year-old girl. Von Monakow produced rapid growth in a fourteen-year-old dwarf with the same substance, and other cases in which the use of this hormone has been effective have recently been reported. As far as I know, the growth hormone is not as yet available commercially, but when it is, its availability will present many perplexing problems to the practicing pediatrist. We will have to decide upon proper indications for its use and answer such questions as "what is a dwarf?" The reviewer feels that the responsibility added to the profession would be so great that this biologic substance should be given thorough trial in established clinics before it is marketed to the profession at large. Perhaps I am overtimorous, but I shrink from the thought that in my declining years I might have to face resentful patients protesting that I had made them too tall or had neglected to make them tall enough.

Pituitary gigantism is a clinical entity resulting from overproduction of the acidophilic cells before the age of puberty, in reality a juvenile acromegaly. The overgrowth of the body is more uniform than in acromegaly, however, because the epiphyses have not yet closed. Sexual function, as might be expected from what we know, is usually decreased.

It is conceivable that this disease might prove amenable to treatment with gonadotropic hormones which tend to close the epiphyses and bring on maturity. Since excessive stature is, in my opinion, a much more tragic situation than being undersized, this subject may well interest the clinician of the future.

Pituitary cachexia, Simmond's disease, has received considerable attention from practitioners treating adults. Silver in his report cites no instance of this condition in a child. However, I have recently had under my care a fourteen-year-old girl who presented this syndrome. She lost 40 pounds in one year, stopped menstruating, showed a basal metabolic rate of minus 30, microsplanchnia, lassitude, and anorexia. After obtaining an increase of symptoms, if anything, with thyroid administration, she immediately improved when given antuitrin subcutaneously, 2 c.c. daily. For a week she gained 1.5 pounds daily and finally has put on 34 pounds; all of her subjective symptoms have disappeared; but to date menstruation has not been reestablished. It would not be surprising to find that some of the more obscure maladies characterized by growth disturbance have their basis in pituitary dysfunction. Premature senility, progeria, bears a marked resemblance to pituitary cachexia.

In all cases of *thyroid* and *adrenal dysfunction* the pituitary factor must be considered because of the marked stimulating effect which the hypophyseal secretions exert upon these glands.

Since *pituitary basophilism,* Cushing's disease, and *acromegaly* occur only in adults, they interest the pediatrist only as they illustrate the multiple effects produced by overactivity of two of the cell types in the anterior hypophysis, the basophiles and the acidophiles, respectively.

Pituitary basophilism is characterized by obesity confined to the head, neck, and trunk, decreased sexual activity, hirsutism, cyanosis, polycythemia, and decrease in the calcium of the bone and in the blood sugar. This disease has always proved fatal in a few years. The symptoms are explained on the basis of basophilic adenoma with over-

production of the gonadotropic hormones, pressure effects, and secondary endocrine abnormalities due to the influence of the pituitary on other ductless glands.

Acromegaly is usually due to adenomatous overgrowth of the acidophilic cells. It results in growth of all parts of the body still capable of responding to the growth hormone. Enlargement is noted in the actral parts, in the periosteum, tongue, skin, nasal cartilages, larynx, and in the hair growth. In women it is customary to state that they become more masculine, exhibiting virulism, an effect presumably due to secondary adrenal stimulation. As is the case in basophilism, pressure effects may cause complications in the picture due to dysfunction of the posterior lobe and of the hypothalamic region of the brain.

Pubertas praecox of pituitary origin and *pituitary eunuchoidism* and *myxedema* have been described but are extremely rare clinical conditions.

It is probable that *dystrophia adiposogenitalis,* Fröhlich's syndrome, and allied conditions will be much better understood as soon as experimental work on the relation of the hypophysis to fat metabolism clarifies the atmosphere. We have all seen so many of these fat, hyposexed children develop into tall, sexually competent individuals without therapy that great care must be used in evaluating reports.

As far as the value of oral administration of pituitary hormones is concerned, there is much difference of opinion. Research workers almost unanimously contend that gland extracts are impotent when given by this route. Yet, many competent clinicians have reported results which seemed favorable. This is one of the many controversial issues which will have to be decided by experience. In the meantime it behooves us to keep an open mind.

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The literature on this subject is so voluminous that even to mention the books, articles, and abstracts consulted in this review would entail hundreds of titles and yet be inadequate from the standpoint of completeness. I am, therefore, listing only the main sources of information, the places from which adequate bibliographies may be obtained.

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American Academy of Pediatrics

Proceedings

FOURTH ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

JUNE 11, 12, 1934

Round Table Conference on Infantile Eczema

Leader: Dr. Lewis Webb Hill, Boston. Assistant: Dr. Irvine McQuarrie, Minneapolis.

CHAIRMAN HILL.—Urbach says in his book, *Skin Diseases and Nutrition*, "Whoever seriously tries to deduce from such a maze of controversial opinions and contrasting personal experiences, any definite conclusions as to the proper treatment of infantile eczema, surely finds himself in a quandary."

He is right for two reasons. First, under the heading "infantile eczema" are grouped a number of different dermatoses. Furthermore, individual skins may react to the same stimulus with different types of eruption or to different stimuli with the same type of eruption. Second, there is no disease in which it is easier to make false observations or to draw incorrect conclusions from true observations—much very unsound material has appeared in the literature.

In spite of the fact that there are included under the heading "eczema" several different conditions, it is probably best for our purposes to include them under one heading, for they are so closely interrelated and one may shade into the other so imperceptibly that it is often not possible to make clean-cut and sharp distinctions until we know a good deal more than we do now.

For the present we may include under the heading "the infantile eczema group" the following conditions:

1. Seborrheic dermatitis
   A. Erythrodermia desquamativa
2. Allergic eczema
   A. Atopic eczema
      (1) Infantile
      (2) Chronic in older children
   B. Contact dermatitis
3. Mycotic eczema*

SEBORRHEIC DERMATITIS

Seborrheic dermatitis is characterized by patches of inflammation with scaling. The scales may or may not be yellow and greasy. There is no vesiculation, and there-

*This, of course should not be called "eczema," but it is so often clinically indistinguishable from chronic eczema and so many times is superimposed upon an atopic eczema that it is probably best to include it in the group.

fore no oozing. It begins usually on the scalp, extending to the forehead and cheeks, or may occur in patches on the body. As regards infants, we may perhaps recognize two varieties: the first corresponding exactly to the adult type, with rather sharply margined patches on the face, chest, or back and the usual scaling. This is not very common. The second, or more common, type, seen especially in young infants, is characterized by greasy scales on the scalp, or "cradle cap," and some involvement of the cheeks and forehead, but not in sharply defined patches. I am not at all sure that we should call this seborrheic dermatitis, but there is certainly plenty of seborrhea of the scalp and dermatitis of the face. This may clear up, or it may develop into a true eczema as the baby grows older, with vesiculation and oozing and wider distribution. It may be often looked upon as the first stage of eczema. Seborrheic dermatitis in its pure form is not an allergic disease, but, on the other hand, since a great many allergic infants with eczema have seborrhea of the scalp, it may be said that in young infants it is often impossible to draw a hard and sharp line.

The dermatologists themselves do not know accurately the etiology of seborrheic dermatitis. From time to time various observers have isolated special fungi and have claimed that it was a fungus disease. Some recent work is by McLeod and Dowling in England,* who isolated a fungus that they call "pityrosporon," and reproduced lesions similar to seborrheic dermatitis, by inoculation with it. This has not been generally accepted by dermatologists, however. The fact that clean-cut, typical cases of the disease are usually cured with sulphur and salicylic acid does indicate its possible parasitic origin, however. In infants, particularly, it is probable that metabolic errors play an important part, but the nature of these is unknown.

As a subgroup under seborrheic dermatitis, we should include that curious and little understood condition, erythrodermia desquamativa, which begins in the first few months of life and is characterized by an intense redness all over the body, usually with a good deal of scaling and always with well-marked seborrhea of the scalp. It is looked upon by Moro as the "hohen typus" of seborrheic dermatitis, because in the milder forms with a patchy, instead of a diffuse, redness they are very similar. In some cases there may be almost no scaling, simply an intense redness all over the body; it may be that these several forms are in reality different diseases, but it seems best for the present to include them in the same group. In the pure form of this condition there is not the vesiculation of true eczema, but I have seen cases of atopic eczema with positive skin tests, which cases were very similar to erythrodermia. It is very likely that an allergic baby with an added marked seborrheic tendency may react with the picture of erythrodermia rather than with the usual scattered vesicular eruption of atopic eczema. In its typical form it is probably not allergic.

No one knows anything about its etiology. The most varied, and sometimes the most fantastic, methods of treatment have been recommended, but here again it is apparent that but little of real value is known. I have had very good results in some cases with a low-fat-and-sugar and high-casein diet. In the cases in which this diet has worked, I have seen the skin clear entirely in from three to six weeks. It is important to pay a good deal of attention to the nutrition of these babies, not to underfeed them, and to start a full mixed diet as soon as possible. They cannot be cured by any local treatment, and boric acid ointment or vaseline with salicylic acid does as well as anything.

ALLERGIC ECZEMA

For the discussion of eczema allergy may be defined as a condition of hypersensitiveness to substances to which normal individuals are not sensitive.

*Brit. J. Dermat. 40: 139, 1928; 42: 562, 1930.

Under the heading "allergic eczema" I would include atopic eczema and contact dermatitis. Atopic eczema is often hereditary, may be associated with asthma or hay fever, and gives positive skin tests to proteins by the scratch or intracutaneous method; also reagins in the blood can often be demonstrated by passive transfer.

A baby two or three months old begins to have seborrhea of the scalp and an eruption on the cheeks, which soon becomes vesicular and oozy and spreads to the outer sides of the lower legs or to any part of the body. In the beginning in very young infants skin tests to proteins may be negative (shown so well by Smyth), but as the baby grows older the tests become positive, particularly to egg.

This is a very important and interesting baby because, since he represents the very first stages of allergy, it is always instructive to study any disease condition in its primitive form. He may have eczema for a while and recover from it spontaneously; he may be cured by intelligent treatment; he may develop chronic eczema with multiple sensitivity and have it for years; or he may develop hay fever or asthma with or without the eczema and be an atopic individual the rest of his life.

About two-thirds of all cases of eczema in infants and children are atopic. Skin tests to proteins are of very considerable value in dealing with this group. As you all know, there has been a great deal of discussion as to whether the cutaneous or intracutaneous test is more valuable. More recently the passive transfer test has come into the field. It has seemed to me that the cutaneous test is the best, for many reasons, in dealing with infants and children. If the same concentration of atopen is used, there is no question that the intracutaneous test is more delicate; but in cutaneous testing a very concentrated solution is ordinarily applied, and, if done properly, it should very closely parallel testing by the intracutaneous method.

In very sensitive infants generalized reactions are not uncommon with the intracutaneous test, and I was told in New York recently that in the last year there had been three fatalities there as a result of this test. The method of passive transfer may be used occasionally if an infant's skin is covered with eruption too much for scratch tests, but is not very practical for general use and applies more to certain special cases or to investigative work than it does to routine work in the clinic or office.

For infants the most common allergens giving reactions are egg, wheat, and milk. In older children sensitivity to foods tends to lessen, and sensitivity to epidermals takes its place, notably cat hair.

Skin tests have been found positive by various observers in from 40 per cent to 80 per cent of different series of cases of eczema. In my own series the incidence is about 60 per cent. If one carefully selects those cases which appear clinically to be of the atopic type, that is, the "true eczema" of Moro, the incidence is higher; he obtained 80 per cent positive reactions to egg white in this group.

The frequency of egg reactions is most interesting, probably very important, and not entirely clear. In my own series, egg reactions occurred in about 55 per cent, and in forty-six infants under six months of age who gave positive tests to something, forty-two reacted to egg, and twenty-four to egg alone, in spite of the fact that they had never eaten egg. In a similar series of forty-six the ages between six and twelve months, only 12 reacted to egg alone, and in another series between the ages of two and twelve years, only eight. It may be taken as a fact, based upon some very accurate work by Moro in Heidelberg and Woringer in Strasbourg, that these egg reactions are due not to some nonspecific irritating quality of egg white, but to a true and specific egg sensitivity. It is evident that these eczematous babies who are egg sensitive and who are not eating egg are not having eczema from the egg, and that egg sensitivity in many cases should be looked upon as an index of allergy rather than as an immediate cause of the symptoms. The origin of this

egg sensitivity is not entirely clear, and it would take too long to discuss the various theories. At any rate, we are confronted many times by infants who have eczema, who are definitely sensitive to egg, who have never eaten egg, and who are apparently sensitive to nothing else so that as far as our therapy goes, we cannot base it upon any specific sensitivity but must be content with local treatment. This group of infants is very important, is but little understood, and needs much further study.

There are several possibilities: 1. Are these babies sensitive to milk, which is the only food they are eating, in spite of the fact that they give negative skin tests to milk? It is true that in some cases the eczema is cured by a milk-free diet in spite of negative milk tests?

2. May it be a question, not of sensitivity to milk, but that in these egg-sensitive babies the egg sensitivity has done something to the skin cells which enables some constituent of the milk to produce the eczema in a metabolic rather than in an allergic manner?

3. Is it possible that these babies are sensitive to some external allergen, such as some of the epidermals, and that if one is intelligent enough he can discover the external allergen which is at fault? Because pediatricians are also dietitians, we have focussed too closely on the dietetic origin of infantile eczema and not enough on external factors, although in infants positive skin tests to external allergens are not very common. Dr. Peck as a dermatologist, perhaps overestimates the importance of external allergens and minimizes food; I do not agree with him in his method of testing or with some of his conclusions.

In the present state of our inadequate knowledge, we find a good many young eczematous babies with positive tests to egg and to nothing else that they are eating or coming into contact with. For some of the more severe cases a milk-free diet is worthy of a trial and is sometimes very successful. If this is not successful, we are confined to local treatment.

If there are found positive tests to any food which the child is eating, withdrawal of that food is indicated; in many cases results are excellent. This is particularly true in cases of wheat or milk sensitivity. Not infrequently, however, multiply sensitized infants will give positive reactions to so many foods, that if they were all withdrawn not much would be left. In these cases withdrawal of what seem to be the most important ones is the best plan to follow, for it is by no means true that positive tests in a multiply sensitized child always indicate that the foods or other allergens which give positive tests are causing the eczema. In strongly allergic children almost any protein which is absorbed through the intestinal mucous membrane in an unsplit condition may produce changes in the skin cells which make positive skin tests possible.

The question of the relation of cow's milk to infantile eczema is a very important one, but much further work is necessary before it can be thoroughly understood. Cutaneous tests to milk are positive in about 17 per cent of infants, in about seven per cent of older children. For the infants the withdrawal of milk and substitution of a milk-free food is likely to be very satisfactory. Since milk sensitivity is almost always outgrown, after a few months of freedom milk can usually be resumed. The cases with negative milk tests are harder to understand, for also in some of these withdrawal of milk is followed by a cure of the eczema. Inasmuch as most of these infants react to egg, it is certain that they have the type of skin which is capable of giving positive skin tests; it seems as though they should react to milk if they are really sensitive to it. It may be that these babies are not sensitive to milk at all, but that other factors in milk, of which we know nothing, enter into the picture.

Although the caseins of cow's milk and goat's milk are very closely related and skin tests to goat's milk are usually positive when cow casein is positive, some babies are able to take goat's milk without allergic symptoms when cow's milk causes the symptoms. The allergenic powers of lactalbumin are much reduced by prolonged heating, and, if the sensitivity is to lactalbumin alone, it may be possible to feed a lactalbumin-sensitive baby on ordinary milk which has been boiled a long time, on evaporated milk, or on the proprietary "hypoallergic milk." The allergenic powers of casein, however, are changed little if at all by heating; if there is sensitivity to casein, a milk-free diet is indicated. I much prefer it in any case of milk sensitivity —no matter to what constituent of milk the sensitivity may be. The fact that almost all cases of infantile eczema begin when the baby is eating nothing but milk indicates very strongly that if any food is causing the trouble, it is milk. In many such cases, however, a milk-free diet does no good whatever. There is much here that must be worked out. If no food sensitivities can be detected, the feeding of an eczematous infant should proceed the same as the feeding of any other baby.

As regards so-called external allergens, I have seen cases that were possibly due to silk, to wool, to dog hair and cat hair, and, as I said before, it would be well for us all to pay more attention to these and to other external allergens as possible factors in the future. My feeling at present is that they are not as important as internal factors, i.e., **food.**

It must be remembered that if an infant is strongly sensitive to such things as silk, orris and feathers, it is not necessary for these substances to come into external contact with the skin in order to cause eczema—they can enter by way of the respiratory tract and cause skin symptoms in this way. These allergens may be then in reality not external in their action at all. This, though not generally appreciated, was brought out by Figley and Parkhurst last year.

In older children atopic eczema takes a somewhat different form. It is characterized by papulation and infiltration rather than by vesiculation and is most often seen back of the knees, in front of the elbows, and around the neck. It has been called by various names, especially "neurodermatitis." It is not an eczema histologically; but, since surely it is the same thing the babies had, modified by chronicity and due to the same causes, it is probably best for us to call it "chronic atopic eczema." The general method of approach is the same as for the infants. Sensitivity to foods is not as common as in infants, and sensitivity to epidermals and to other external allergens increases. Multiple sensitization, which is very common, makes specific treatment difficult.

Desensitization, either specific or nonspecific, both in infants and children, has not been found very useful and applies only to a limited number of special cases—perhaps those in which it is not possible to remove an external allergen from the environment and in which the eczema is almost entirely due to this allergen, or in certain cases in which there is very severe sensitivity to some common food. It may sometimes give fairly good results, but it is one of those procedures which sounds better when one is talking about it than it actually works in practice.

CONTACT DERMATITIS

The continental school of dermatology, led by Bloch, of Zurich, and Jadassohn, of Breslau, has for some time regarded eczema in adults as a contact dermatitis, in the same category as our dermatitis venenata. This is allergic, for a state of hypersensitivity exists; but it is not atopic because it is not hereditary, because no reagins are demonstrable in the blood, and because scratch and intracutaneous tests to proteins are negative. The exciting agents are usually of nonprotein nature, such as metals, drugs, various dyes, woods, vegetable oils, and indeed almost any substance with which the hypersensitive person may come into contact. The sensitiza-

tion is of the epidermis rather than of the cutis, and sensitivity is tested for by means of the patch test by which a small amount of the suspected substance is applied to the unbroken skin and covered with adhesive tape. The reaction is a delayed one, and usually appears in forty-eight hours or more. The reaction is not urticarial but is manifested by small vesicles on an erythematous base, and sometimes the sensitivity is so exquisite that severe dermatitis is started by the test. In the acute forms the character and distribution of the eruption usually serve to distinguish it from atopic eczema; in the more chronic forms the two may be very hard to differentiate. Chronic atopic eczema, however, has a predilection for the front of the elbows and back of the knees; contact dermatitis occurs anywhere, but especially on exposed surfaces, such as the face, hands, or forearms. In contact dermatitis there is almost always some tendency to vesiculation; in chronic atopic eczema there rarely is. This conception of eczema and the use of the patch tests were brought to America by the pupils of Bloch and Jadassohn and have been of the greatest possible value in dermatology, more particularly for adults.

In children, if the eczematous process began during the first few months of life, it is almost surely atopic; if it began suddenly on a previously healthy skin at some time during later childhood, it may be of the contact variety. Since very little work has been done with contact dermatitis in babies and children, I do not feel at all certain how common it may be. The infant and young child come into relatively little contact with the things which cause this type of eruption, and it is probably not nearly as important in infants and children as in adults. I have recently seen, however, three cases in young children which were apparently contact dermatitis, two probably from the dye in clothes and one from turpentine.

I have not been able to duplicate Dr. Peck's work with patch tests. In a series of twenty-five cases, using the same technic and the same allergens,* I have had no positive reactions whatever. If this paper is carefully studied, it will be seen that most of his positive patch tests were to feathers. In a group of twenty-five consecutive infants in my clinic with the usual type of facial eczema, I found that fifteen slept on no pillow, four on kapok or cotton pillows, and only five on feather pillows. Practically all of Dr. Peck's babies slept on feather pillows. Furthermore, I have had recently a number of cases with very strongly positive scratch tests to inhalants; cattle hair, silk, cottonseed, and cat hair, and patch tests in these cases gave no reaction whatever. I should, however, like to see a large series with negative scratch tests, tested by the patch method with the same nonprotein substances that are used for adults. The subject of contact dermatitis in infants and young children is practically an unexplored field and needs much further study. The distinction between contact dermatitis and atopic eczema is an important one, and it seems likely that while the so-called "external" protein allergens (cat hair, silk, and cottonseed) may occasionally work by contact, they more often work by inhalation.

MYCOTIC "ECZEMA"

In the last few years fungi have assumed great importance in dermatology, and many eruptions hitherto classed as eczema in adults have been found to be in reality fungus infestations. The two organisms responsible for most of these eruptions are members of the trichophyton group and *Monilia albicans*, the organism of thrush. There are many reports in the literature of yeastlike fungi (cryptococci) having been found in various eczema-like dermatoses, but these forms occur so often on normal skin that their etiologic significance is in some doubt. *Monilia albicans* does not apparently occur on normal skin, and if this is recovered, the chances are that it is the cause of the skin lesions.

*Dr. Peck used the same allergens, in protein powder form, that are ordinarily used for scratch or intracutaneous tests in atopy.

Little has been done as regards the presence of these infestations in infantile eczema. Schamberg in 1915 reported one of the first cases of thrush of the skin in an infant, and Peck has reported a case of trichophyton infestation in a child of fifteen months, but there is practically no information as to how common these infestations may be in what is ordinarily called "eczema."

In the last two years I have been very much interested in this question and have been using the intracutaneous monilia and trichophyton tests routinely. It is too early to make any very definite statements or to be sure of the value of these tests, but so far the work seems to indicate the following:

1. Trichophyton infestation is very uncommon in infants and children and is of little or no importance as a cause of "eczema."

2. Monilia (thrush) infestation may be of some importance either as a primary cause or as a contributing cause of "eczema" in from 10 per cent to 15 per cent of all cases as it occurs in young children.

3. Monilia is probably of no importance in the ordinary facial type of infantile eczema. But, if there are patches of scaly eruption in the groins, or large, rather sharply defined areas on the body, or involvement of the fingers and nails, we should suspect the presence of this infestation.

Knowledge of infantile eczema is by no means adequate, but with the invaluable help of the dermatologists and allergists, the subject has certainly become much less obscure than it was a few years ago. We should follow closely their work with adults and take unto ourselves as much of it as seems applicable to our own particular field.

A few procedures in the therapy of infantile eczema really may work; a great many which are often used can do no good whatever. If we can learn what is useless and prevent ourselves from doing things that are not founded upon sound observation and carefully interpreted facts, we shall have gained a good deal.

DR. IRVINE McQUARRIE.—Dr. Hill's comprehensive review of the subject makes a foundation for any new approach to the subject because he has presented the problem in such a way that we all must have entirely open minds about it. Approximately two years ago Hansen conceived the idea of investigating the possible clinical bearing of a discovery made in 1929 by Dr. George Burr and his wife regarding the requirement in animal nutrition for unsaturated fatty acids. These workers, and almost simultaneously Mendel and his colleagues, discovered that rats placed on completely fat-free diets which were adequate in all other respects soon developed a definite syndrome characterized in the early stages by scaliness of the skin and in the later stages by cessation of growth, necrosis of the tail, and pathologic alterations in the kidneys. Burr found that when he added certain fats to the diet of these experimental animals, they again began to grow and the skin scaliness disappeared entirely. He later found that the essential substances are the unsaturated fatty acids in the fat, such as linolic, linoleic, and possibly arachadonic acid, which have double bonds in their molecules.

Hansen empirically began feeding linseed oil to certain eczematous babies receiving no other form of therapy. After a period of a few weeks he found that several babies whom he was treating by this method in the out-patient department were very much better. Since patients with eczema are not so common, he could not investigate this observation as fast as he wished. Therefore, he obtained samples of blood from rats fed on fat-free diets in Dr. Burr's laboratory and on these determined the total iodine absorption values of the serum and the iodine number of the serum fatty acids as he had previously done in the case of normal and eczematous infants. He found in a short time that he was getting very low values in the experimental rats just as he had in the eczematous infants.

New eczema patients have been taken into the hospital where he could make careful clinical observations and at intervals determine the iodine number of the serum fatty acids in duplicate. To date over thirty of the patients studied in this manner have been found to have lower iodine absorption values during the active phase of the disease than normal control subjects of similar ages.

A large majority of these patients have shown marked improvement with no treatment other than feeding them linseed or corn oil, that is, products high in unsaturated fatty acids, and restraining the limbs to prevent scratching. Accompanying this clinical improvement Hansen has found the iodine absorption value of the serum to increase from subnormal to essentially normal levels.

In a few cases he has tried the effect of tar ointment, a standard form of local treatment which is recognized as being very effective in clearing up the skin lesions temporarily. These patients as well as those subjected to the oil treatment were kept on the regular ward diets. He found that these patients, when successfully treated with tar, showed a similar increase in the serum unsaturated fatty acids.

These observations do not tell, of course, whether this phenomenon that Hansen has observed is the result of the eczema or whether it is an underlying basic factor in the etiology. Certainly we have continued to look, as Dr. Hill pointed out, for general constitutional systemic factors rather than just local factors, that is, for some reason why these babies have eczema where the normals do not. I think that the factor of allergy has satisfied most people, but I can see that it does not satisfy Dr. Hill; nor does it seem to me to meet all of the requirements of a satisfactory theory because I have had similar unsatisfactory experiences with patients. We get patients who have skin sensitivity and who do not improve after withdrawing from the diet the material to which they are skin sensitive. Again we see babies responding well to withdrawal of other substances to which they are not skin sensitive. While allergy is a constitutional factor that one can hardly escape, there may well be others of equal importance, such as the dietary factor that I have discussed here.

It is rather interesting that von Groer, of Vienna, in the course of studies on the relative nutritive values of carbohydrate and fat kept two babies for periods of several months on fat-free diets. It was noted incidentally that one of the babies developed what he called an "exudative diathesis" at the end of three months. The author comments about this in a semihumorous way to the effect that this observation was rather odd in the light of Czerny's claim that fat intolerance is an etiologic factor in infantile eczema. It appears that what he actually did was to deprive these patients of unsaturated fatty acids for one thing. The effects of fat-free diets have not been reported by other observers, as far as I know. One of our colleagues volunteered last winter to go on a fat-free diet and has remained on it for approximately six months now. I have examined him semiweekly for any change whatsoever that might result, but clinically he has remained entirely normal. His iodine number has fallen from 122 to 95. Whether, after he has been on it for another few months, he will develop skin eruptions or not cannot be predicted. I doubt whether he will show anything; he feels perfectly well and is getting along satisfactorily. That does not prove anything as regards the growing infant, of course. We know that an adult kept indoors on a diet free of vitamin D does not develop rickets of the infantile type. Osteoporosis finally develops, but not typical rickets. Thus, our adult subject may not develop eczema under conditions favoring its development in an infant.

As regards the mechanism of local treatment with tar ointment, we cannot speculate too much, but it is interesting to note the fact recorded by Hendel and Malet, of Montevideo, that application of tar ointment to the skin of mice produced an increase in the neutral fat of the liver and certain changes in the skin lipids. This discovery points to a generalized or constitutional effect. These results, together

with the observation that application of tar ointment to one eczematous area of skin is often followed by improvement of areas not treated, indicate that there is a constitutional effect from local application. Some have argued that coal tar has no specific effect at all because control areas of skin, to which it is not applied, often improve as well as those treated, but one can interpret it just as well the other way.

I would like to say, in conclusion, regarding this preliminary work on the relationship of fatty acid metabolism to infantile eczema, that no rigid claim is made for it as a final word regarding etiology or as a panacea for all eczematoid lesions. The observation is simply recorded that there is a disturbance in the unsaturated fatty acids of the blood plasma in many cases. I think you will agree with me that it is a rather promising lead for approaching the problem from a new angle. Undoubtedly, as this is tried all over the country with inadequate doses of oil, we are going to have some discordant results. There will be overenthusiasm in some quarters and discouragement in others as with all new procedures, but I believe that some genuine advance toward solution of the eczema problem is in the offing in this direction.

DISCUSSION

DR. JOHN RUHRÄH (BALTIMORE, MD.).—I would like to ask Dr. McQuarrie how much oil he gave, was it taken and tolerated well, and whether olive oil would be borne better? Did the infants get entirely well?

DR. McQUARRIE.—We cannot say what the optimal dosage is yet, but usually it is in the neighborhood of an ounce a day—all the way from half an ounce to two ounces a day in babies ranging from five to eighteen months. Sometimes part of the fat in the milk is removed and the oil whipped with the milk, at other times it is fed with cod liver oil.

The effect, clinically, is fairly striking. There was one recurrence, within a period of about twelve days. The baby went home clear and came back erupted again. There may be some external factor, but his iodine number had gone down from about 111 to 85. Whether the eczema had produced the low iodine number, or whether the fact that he had discontinued the oil some time previous to leaving the hospital and had had no more, I don't know. Dr. Hansen has had other patients who have gone five months without showing any recurrence. He has had some who have been free from eczema for considerably over a year.

CHAIRMAN HILL.—Did you use a purified linseed oil?

DR. McQUARRIE.—It is raw linseed to avoid lead, as occurs in the process of "boiling."

CHAIRMAN HILL.—Have you ever used that special artists' oil that is pure white?

DR. McQUARRIE.—Dr. Hansen has used raw linseed oil obtained for this special purpose by our hospital drug department.

CHAIRMAN HILL.—Is the corn oil fairly efficient if you give enough of it?

DR. McQUARRIE.—Yes, it is; edible oils are probably all less effective than the linseed oil, the effectiveness apparently being directly dependent upon the content of linolic acid. The iodine number, which measures the degree of unsaturation of the fatty acids, runs from 20 to 30 in ordinary cow's milk fat, and from 40 to 60 in breast milk. That of linseed oil varies between 160 and 200. Other oils show intermediate values.

One should be sure that the linseed oil is obtained from sources excluding contamination with mustard seed and that it does not contain lead, which is said to be present in some samples, because of the method used in its manufacture.

DR. PHILIP BARBA (GERMANTOWN, PA.).—What is the rank of cod liver oil?

DR. McQUARRIE.—While cod liver oil has a comparatively high iodine number, it is not very efficient in curing the disorder in rats on the fat-free diet. This is said to be due to the fact that the unsaturated acids are not the same as those in linseed oil and do not have the same rôle in the metabolism of the animals. Many babies getting ordinary cod liver oil in doses of three teaspoonfuls a day have eczema. This amount is not enough; apparently more than three teaspoonfuls a day is needed. I have often seen rather large square heads, suggestively rachitic in appearance, in rapidly growing babies with eczema. Some balanced studies ought to be made in such babies to determine whether or not fat and its contained accessory substances are absorbed efficiently.

DR. RUHRÄH.—Are these the flabby, fat variety?

DR. McQUARRIE.—Mostly fairly well-nourished babies, but flabby like the rapidly growing baby with mild rickets.

DR. RUHRÄH.—Have you tried it on older children with eczema?

DR. McQUARRIE.—Yes, but the results are not as striking in older children. Dr. Hansen has treated one five-year-old patient at home and then in the hospital without definite improvement. That child happens to have a normal serum fatty acid iodine number.

DR. RUHRÄH.—How about the children who recover about that period anyhow, whether anything is done for them or not?

DR. McQUARRIE.—Certain cases of infantile eczema improve spontaneously anyway. But a large majority of the twenty-five or thirty cases which he has studied so far have shown low serum iodine absorption values when they were in the active phase, and normal or nearly normal values after the skin was entirely clear.

DR. RUHRÄH.—Did you cure your control afterward?

DR. McQUARRIE.—Yes, he did well on linseed oil supplements and finally showed a normal serum iodine absorption value.

CHAIRMAN HILL.—I have seen very little effect from cod liver oil one way or the other. The cod liver oil has been omitted empirically in many cases without any effect at all before I have seen the patients.

DR. ALAN BROWN (TORONTO, ONTARIO).—I have had a number of cases in which, after elimination of the viosterol, which contains corn oil, the eczema disappeared; after the addition of the viosterol again, the eczema reappeared. I saw similar case reports by Balyeat. At first we didn't like to use the linseed oil because of the odor, but the corn oil in doses of about an ounce and a half or two ounces didn't appear to have much effect. When we changed to linseed oil, there seemed to be a very appreciable effect.

DR. BARBA.—I would like to ask Dr. McQuarrie if any allergic tests were made on these children.

DR. McQUARRIE.—Yes, the allergic skin tests were made in all, and a majority reacted positively. Some of these cases were in older infants who had been "the rounds," therapeutically speaking, without success.

DR. BARBA.—Did the allergic patients do well with the oil treatment?

DR. McQUARRIE.—So far as we observed, there was no difference in them, but we have not as yet had enough cases to determine variations in response in relation to other factors. If we could have six or eight hundred patients, as Dr. Hill has followed and could perform tests on them alternately, putting one patient on this and another on standard treatment for comparison, and then could regroup them or classify them in some way, we would learn more about it. This remains to be done.

CHAIRMAN HILL.—It is of great importance in using oil to try to find out in what type of case it really works best. The virtue of this treatment, to my mind, is that it is perfectly harmless. The trouble with so many of the "cures" for eczema appearing in the last twenty-five years has been that they might do harm to the child and they are not very likely to work either.

I have made a list of the different "cures" for eczema that have been produced during the past fifteen or twenty years:

1. Czerny's, low fat diet
2. Finkelstein's, low fluid and low sodium chloride
3. Scheer's, hydrochloric acid milk
4. Schiff's milk-free diet
5. Atropine injections
6. Superheated milk
7. Injection of urinary proteose
8. Autohemotherapy
9. Injections of boiled milk

Besides those eight there are doubtless more. None of these have stood up, and most of them do a certain amount of harm to the child. There is one great virtue about your treatment—it is founded upon scientific observations in the beginning; in the second place, it is a perfectly harmless procedure.

I suggest that during the next year we all use it as much as we can and keep careful records as to what type of case we use it in especially, and we will all report upon it a year from now.

DR. McQUARRIE.—Regarding the lack of relationship of allergy per se to the serum fatty acids, Dr. Hansen has found that the serum fatty acids of patients with asthma and hay fever have perfectly normal iodine numbers. A small group of six or eight older children who had had infantile eczema at one time and then as time went on had developed asthma or hay fever as well as mild chronic eczema did have iodine numbers averaging 105.

CHAIRMAN HILL.—Do you think it would be a fair test if we used an ounce and a half of corn oil? I am rather inclined to corn oil than the linseed oil.

DR. McQUARRIE.—I am not sure; there may well be individual variations. Some patients may respond on half an ounce. I should think that one to one and a half ounces would be sufficient, particularly if linseed oil is used, as in Dr. Brown's experience. Our babies really take linseed oil quite well.

DR. BARBA.—How about the possibility of isolating the acids?

DR. McQUARRIE.—That is being worked on at the present time. Several other aspects of the problem are also being worked on. One of these is that of determining the iodine number of the fatty acids of breast milk from mothers with eczematous babies for comparison with the breast milk of mothers with normal babies.

I would say, in general, Dr. Hill, if people who take this up will work with the same method that Dr. Hansen has used and run iodine number determinations on

their eczematous babies, securing normal controls at the same time, we shall learn more about it than we ever can by working haphazardly. Patients like one little boy who is in our hospital at the present time with an eczematoid eruption may not respond to oil administration, but they differ from those who do in having normal serum fatty acid iodine numbers. Infection ought also to be noted. We had in the hospital for several months an eczematous patient with otitis media and infection around her ears and in the cervical glands with a relatively low serum iodine number in spite of nearly two ounces of linseed oil a day. Following the disappearance of the infection, the skin gradually cleared, and the iodine number of the serum fatty acids returned to normal.

CHAIRMAN HILL.—Infection can work in two ways; it is very common to see a baby with very severe eczema get some sort of infection with a high fever and have his eczema disappear overnight. We have all seen that, and then, when he gets rid of his infection and fever, the eczema comes back the same as before. Not infrequently during acute upper respiratory infections a baby or young child will have hives, and it is also true that if there is a chronic focus of infection anywhere in a child with eczema, it is a very good plan to clear it up. I don't believe that infection accounts for the underlying process in most cases.

DR. McQUARRIE.—Hansen uses the Page, Pasternoch and Burt modification of the Rosenmund-Kuhnherin method for his iodine number determination. It is quite an easy technic for chemists who do that work in the laboratory.

DR. FRED RITTINGER (CLEVELAND).—Have you ever used soy bean oil?

DR. McQUARRIE.—Not since this study has begun. Sobee, which Dr. Hill introduced, contains nearly all the fat as olive oil.

DR. RITTINGER.—What is the iodine number of soy bean oil?

DR. McQUARRIE.—I do not know.

DR. WARD E. COLLINS (KALAMAZOO, MICH.).—Have you seen children with eczema for a long time who fail to grow and gain and who seem to be suffering from an infection with considerable glandular enlargement and fever?

CHAIRMAN HILL.—Yes, I think that applies particularly to chronic cases in children from a year to three years old with general glandular enlargement, very red skins; they are pretty miserable children all around. There is some underlying process going on which we don't understand.

DR. BARBA.—Rotner found that, if the mother was inoculated with horse serum late in pregnancy, a passive transfer developed in the individual offspring a varying period after birth which transfer was lost as the child grew older.

CHAIRMAN HILL.—That is much what happens in atopic eczema. The child is born normal and doesn't begin to have eczema until he is three or four months old. He is eating nothing but milk but is apparently sensitive only to egg.

Has anyone any suggestions or ideas to offer as to the local treatment of eczema? Or have any of you had any experience with hypoallergic milk?

For some time in every case of milk sensitivity which gives good reactions to casein, or lactalbumin, I have been testing also with goat's milk and human milk; with milk heated to 130° C. with casein amynoids, a digestion product of casein, and milk peptone, a digestion product not broken down as far. Almost all patients who give reactions to cow's milk will react to goat's milk, and most patients who react to casein will react to the heated milk as strongly as they do to unheated milk. If I have a case of real milk sensitivity, I very much prefer

a milk-free diet rather than trying to get around it in any other way. Although if there is only a lactalbumin sensitivity, evaporated milk is often indicated, and I like to use it as a routine feeding anyhow for many cases. It is very easily digestible.

I don't use sobee a great deal except in milk-sensitive cases; sometimes for very bad cases, not of milk sensitivity, it does well. As regards various milk formulas—shifting around from one type to another does not make enough difference to amount to anything.

DR. DONALD C. MEBANE (TOLEDO, OHIO).—I continually underfeed the infants a little and give them variety in order to prevent infantile eczema.

CHAIRMAN HILL.—Overfeeding is a very potent cause of eczema.

I think we get better results with crude coal tar locally than with any other one thing. But it is black and dirty. Within the last few months we have used a white tar, different from any of the other white tar preparations, which may amount to something.

DR. E. G. PADFIELD (SALINA, KAN.).—I would like to ask Dr. McQuarrie if using the crude coal tar locally raises the iodine number any appreciable degree?

DR. McQUARRIE.—In the few observations made so far the iodine number has been low to begin with and, after the patients had been treated with crude coal tar preparations and the eczema had cleared up, the iodine number had increased. Whether it is the tar or whether there is some indirect factor that raises it as the patient gets better, I could not say.

DR. PADFIELD.—In the light of your work, my treatment of these patients seems terrible. I had been firmly convinced that fat probably caused more harm in the eczematous children than proteins; consequently, I have put them on a fat-free diet and used coal tar ointment with apparently good results.

DR. McQUARRIE.—It may be that the coal tar is doing that.

CHAIRMAN HILL.—Perhaps I can answer that to a certain extent. The first idea of the harmful effects of fat in eczema was brought out by Czerny with his "exudative thesis." If a baby is grossly overfed with fat, taking away some of the fat will do him good, but nowadays with whole milk mixtures instead of cream mixtures, no baby is grossly overfed with fat. The effect is not directly on the eczema, but on the nutrition of the skin. The type and intensity of eruption is dependent upon the nutrition and chemistry of the skin. Some babies will show one type of eruption and some, another type, for that particular reason.

In certain fat babies who have probably a good deal of fat in the skin and the seborrheic type of eczema with fatty, greasy scales, getting rid of some of the fat in the diet will do them good. Getting rid of the fat in the usual baby who isn't overnourished, does not do a great deal of good.

DR. A. B. GROSSMAN (CLEVELAND).—Do you find that by taking children away from their homes, especially the poorer homes and hospitalizing them, their eczemas, especially of the infectious type, clear up without any treatment, just by altering the hygienic care?

CHAIRMAN HILL.—Positively; I am sure of that. The question of taking eczematous babies into the hospital is not easy to decide. They pick up infections quickly and are very likely to die. We have had some very unfortunate experiences with several eczematous babies in hospitals. Dr. Schwartz has written a good deal about it, as you know.

PEDIATRIC SERVICE IN GENERAL HOSPITALS

Report of the Committee on Hospitals and Dispensaries of the American Academy of Pediatrics (Continued)

THE second report concerns hospitals in Region II of the American Academy of Pediatrics. Only hospitals having at least twenty-four beds for children are considered. Bassinets are included in the pediatric service when that service is under the direction of a pediatrician.

Region II represents the states of Alabama, Florida, Georgia, Kentucky, Louisiana, North Carolina, Oklahoma, South Carolina, Mississippi, Tennessee, Texas, Virginia, and West Virginia. In this entire region there are only twenty-one hospitals having an infants' and children's service of twenty-four or more beds and bassinets.

The following Table I gives the distribution of the respective services by states and the relative sizes of these services.

In twelve states and among twenty-one hospitals, all of the services combined have a total bed capacity of 1,162; bassinets, 601. The largest number of beds in any one hospital is 215; the smallest, 18. The largest number of bassinets is 75; the smallest, 12. Two hospitals do not include bassinets in their report and apparently do not have them. In no state are there more than three 24-bed services. Kentucky and Tennessee each have three. All others have only one or two.

Residents.—Ten of these twenty-one hospitals employ a full-time pediatric resident. One employs two residents. All pay the resident a salary which varies from $25 to $80 per month. In four instances the pediatric resident does not serve exclusively in the pediatric department.

Table I

STATE	NO. OF HOSP.	TOTAL BEDS	TOTAL BASSINETS	LARGEST NO. OF BEDS IN 1 HOSP.	SMALLEST NO. OF BEDS IN 1 HOSP.	LARGEST NO. OF BASSINETS IN 1 HOSP.	SMALLEST NO. OF BASSINETS IN 1 HOSP.
Ala.	2	87	63	48	39	40	23
Fla.	2	54	58	30	18	40	18
Ga.	1	38	--	38	38	--	--
Ky.	3	150	127	90	30	75	26
La.	1	143	69	143	143	69	69
N. C.	2	88	74	56	32	50	24
Okla.	1	215	17	215	215	17	17
S. C.	1	50	--	50	50	--	--
Tenn.	3	115	62	56	29	30	12
Texas	2	115	54	80	35	30	24
Va.	1	32	55	32	32	22	22
W. Va.	2	75	55	40	35	30	25
Total	21	1.162	601				

Internes.—Four hospitals offer a special interneship in pediatrics. Sixteen offer rotating interneships in which part of the time is spent exclusively in pediatrics. The usual period of the latter service is one, one and one-half, or two months.

Attending Staff.—Eighty-five pediatricians comprise the attending pediatric staffs of the twenty-one hospitals. The number for states varies from three to sixteen, but only four report eight or more. The period of the respective services varies from two to twelve months. Only one hospital reports a service as short as two

months. The majority of the services are for six to twelve months, but six report services of three- or four-month periods.

Newborn Service.—Fourteen hospitals maintain their newborn service under the supervision of the pediatric department.

Nursing.—There is a special nurse in charge of the children's department in each hospital. Fifteen of these nurses have had special pediatric training. Among a few, this training has been for a period of only two, three, or four months. Nineteen hospitals have student nurses. Their average time of service usually is from two to four months. The average student nurse has from two to ten infants under her care, and, when she is in the children's department, she will care for from three to ten children.

Social Service.—Seven hospitals have a special social service for children.

Diet Kitchen.—Fourteen hospitals have a special diet kitchen for infants, and eleven have one for children.

Schooling and Recreation.—Schooling for convalescents is provided in four hospitals, and recreation in five.

Dispensaries.—Nineteen hospitals maintain a dispensary for children. With only a few exceptions these clinics are open daily with attendance varying on the average from twenty-five to fifty patients. In a few instances the attendance figure is from ten to twelve patients. In fourteen instances the same staff serves in both hospital and dispensary. Residents serve in the dispensary in six of the ten hospitals having residents, and internes serve there in thirteen instances.

Table II presents figures concerning admissions, deaths, autopsies, and percentage of deaths and autopsies.

TABLE II

YEAR 1933

STATE	NUMBER ADMITTED		DEATHS		AUTOPSIES		PERCENTAGE		PERCENTAGE	
	NEWBORN	CHILDREN	NEWBORN	CHILDREN	NEWBORN	CHILDREN	NEWBORN DEATHS	NEWBORN AUTOP.	CHILDREN'S DEATHS	CHILDREN'S AUTOP.
Ala.	2,097	2,317	84	163	18	40	4.0	21.4	7.3	24.5
Fla.	1,028	430	25	71	4	13	2.4	16.0	16.5	18.1
Ga.	1,434	883	38	52	5	11	2.6	13.1	5.8	21.1
Ky.	2,298	2,596	136	229	50	68	5.4	36.7	8.8	29.7
La.	3,102	13,277	171	426	No reply	No reply	5.5	--	3.2	--
N. C.	615	1,143	32	62	26*	41	5.4	81.2*	5.4	66.1
Okla.	369	1,379	45	156	10	67	12.1	22.2	11.3	42.8
S. C.	521	901	41	91	5	14	7.8	12.1	10.0	15.3
Tenn.	1,350	1,181	86	125	19	52	6.3	22.0	10.5	43.2
Texas	866	1,142	62	176	10	35	7.1	16.1	15.4	19.8
Va.	246	376	8	15	2	5	3.2	25.0	3.9	33.3
W. Va.	586	1,050	17	45	2	10	2.9	11.7	4.2	22.2
Total	14,512	26,675	745	1,631	151	354	5.1	20.2	6.1	21.7

*Includes necropsies on stillborn.

COMMENT

Comment will be restricted to this report without comparison with the figures of the first report. Comparative figures from all regions will be discussed in a final report.

The fact is somewhat surprising that in this large area comprising twelve states, only twenty-one hospitals with pediatric services large enough for consideration in this report are found. Furthermore, among these hospitals there is a seemingly low total of 1,763 available beds and bassinets for infants and children. Several factors probably influence these figures, among them, the economic status, population density, and possibly some backwardness in developing better pediatric departments in the hospitals in this region.

Six hospitals have a pediatric department which they consider large enough and of sufficient importance to warrant the employment of a full-time resident. Ten report that they have a pediatric resident, but in four instances he does not serve exclusively in the pediatric department.

Four hospitals offer special pediatric interneships, and among sixteen institutions offering a pediatric service as part of a general rotating interneship, the usual time spent on the service is from one to two months. A rather limited pediatric knowledge would be acquired in one or even two months.

All hospitals have attending pediatricians. There is a total number of eighty-five for the entire area, or about four per state. There are considerably more than eighty-five pediatricians in Region II. Allowing for a large group who confine their hospital staff associations to children's hospitals, there must remain another considerable group who do not have an opportunity to serve in pediatric departments of sufficient size to afford them valuable experience.

Newborn services should be under the complete or at least partial supervision of the pediatric department but are not in seven of these institutions.

Nursing is apparently supervised in each of the twenty-one pediatric services by a graduate nurse. However, according to our information, six of these nurses have not had pediatric training, and among a few their special pediatric training has been for two short periods of time to be of much value.

Pupil nurses are trained in nineteen hospitals, and the extent of their pediatric training is about the same as that in any general nursing course, that is from two to four months.

One-third of the hospitals maintain a social service department for children; two-thirds, a special diet kitchen for infants; one-half, a diet kitchen for children. These figures are gratifying when one considers that many of the children's services are relatively small.

Schooling and recreation for convalescents do not receive much emphasis among these hospitals. Less than one-fifth provide schooling, and less than one-fourth, recreation.

All hospitals but two maintain a children's department in the dispensary, and in general the attendance is good, often being thirty or forty children per day. In two-thirds of the hospitals, the same pediatric staff serves both hospital and dispensary, but internes and residents are in service there in too few instances.

You may draw your own conclusions after perusal of Table II. We merely point out that the total number of children and newborn receiving care in these hospitals during one year is not large. The newborn death rate is commendably low in some and much too high in others. The autopsy percentage figures for both children and newborn show considerable room for improvement in most instances.

Academy News

The Region I meeting of the American Academy of Pediatrics will be held Friday and Saturday, Oct. 11 and 12, 1935, at the Bellevue-Stratford Hotel, Philadelphia, Pa.

Dr. S. Herman Lippitt, Milwaukee, Wis., who had just been elected to Fellowship of the Academy Dec. 1, 1934, died suddenly Dec. 7, 1934, of heart disease.

Dr. Roger H. Dennett, New York, N. Y., died of heart disease Feb. 3, 1935. Dr. Dennett was born fifty-eight years ago in Boston and took his medical degree at Harvard University. He was the author of several books and a contributor to the Journal.

Dr. E. J. Huenekens, Minneapolis, has accepted the state chairmanship for Minnesota.

Erratum

In the article, "A Statistical Analysis of Whooping Cough Cases," by John A. Toomey, M.D., which appeared in the September, 1934, JOURNAL OF PEDIATRICS, the last sentence in paragraph 2 should read, "In our series, 87.7 per cent (instead of 87.3 per cent as published) of the deaths occurred during the first two years . . ."

News and Notes

The eleventh session of the International Association for the Promotion of Child Welfare will be held at Brussels, July 25 to 29, 1935.

There will be four sections: social, juridical, pedagogic, and medical. Among the questions for discussion at the medical section are: The status and needs of pediatrics in the medical organization; infant mortality caused by the diarrheas; immunization against tuberculosis in infancy; and the training of the infant.

The meeting will be held in connection with the International Exposition in Brussels in 1935. Detailed information may be obtained from the secretary, Dr. J. Maquet, Ave. de la Toison D'Or 67, Brussels.

The pediatricians of Louisville under the auspices of the American Academy of Pediatrics will give a practical postgraduate course in pediatrics on each Wednesday beginning April 24 and running through to July 1. The lecturers will utilize the patients in the Children's Free Hospital where the course will be held. The hours will be from 9 to 12 A.M. and from 12:30 to 1:30 P.M. which will enable men living from 75 to 100 miles from Louisville to put in intensive work and get back home in time to take care of any necessary calls. The charge of the course will be $5. Correspondence should be directed to Dr. Philip F. Barbour, state chairman.

The Children's Free Hospital also extends an invitation to any doctor visiting Louisville to spend a day or week in the hospital wards getting acquainted in this way with the newer developments in pediatrics.

The following men have been certified by the American Board of Pediatrics since the last report:

Edward Dyer Anderson, Minneapolis, Minn.
William Willis Anderson, Atlanta, Ga.
Harry Calvin Berger, Kansas City, Mo.
Urban J. Busiek, Springfield, Mo.
Gerald M. Cline, Bloomington, Ill.
William Orlin Colburn, Lincoln, Neb.
Joseph B. Cowherd, Kansas City, Mo.
Vincent Del Duca, Camden, N. J.
Daniel James Dolan, New York, N. Y.
David Gingold, Brooklyn, N. Y.
Roy Edward de la Houssaye, New Orleans, La.
A. Wilmot Jacobsen, Buffalo, N. Y.
Carl O. Kohlbry, Duluth, Minn.
Peritz M. Kurzweil, New York, N. Y.
Sylvan Daniels Lazarus, Brooklyn, N. Y.
Robert Holmes McBride, Sioux City, Iowa
Ralph W. McKelvy, Los Angeles, Calif.
Ellsworth Moody, Joplin, Mo.
C. Ulysses Moore, Portland, Ore.

Ralph E. Netzley, Pasadena, Calif.
Henry C. Niblack, Chicago, Ill.
John Mott Rector, San Francisco, Calif.
Phillip Elias Rothman, Los Angeles, Calif.
Henry Larned Keith Shaw, Albany, N. Y.
Donald C. Shelby, Los Angeles, Calif.
Carl H. Smith, New York, N. Y.
Oliver Linwood Stringfield, Stamford, Conn.
Sidney H. Weiner, Boston, Mass.
Edwin Theodore Wyman, Boston, Mass.

Book Reviews

An Atlas of Infant Behavior. ARNOLD GESELL, PH.D., M.D., SC.D. Volume I, Normative Series (in collaboration with Helen Thompson and Catherine S. Amatruada); Volume II, Naturalistic Series (in collaboration with A. V. Keliher, F. L. Igg, and J. J. Carlson). Loose leaf with over 3,000 photographs. Yale University Press, New Haven, 1934.

Infant Behavior, Its Genesis and Growth. ARNOLD GESELL AND HELEN THOMPSON, McGraw-Hill Book Company, Inc., New York, 343 pages, 1934.

This Atlas is an outstanding contribution in the field of infant behavior. It is not only a unique but a most important contribution. All students of infant development and behavior are familiar with Dr. Gesell's work and methods of study. In these two volumes some 3,000 action photographs have been selected from the thousands of feet of film records made in recent years by Dr. Gesell and his associates in the Clinic of Child Development at Yale University.

Volume I, *Normative Series*, portrays the systematic development by lunar month intervals of postural development, locomotion, and various forms of adaptive behavior; thus the behavior pattern of the infant in the prone, sitting, and standing positions is shown month by month. Such adaption patterns are shown as the use of the cup, and cubes, as well as more complicated patterns in older infants, as the use of ring, string, and bell. A study of the pictures shows the growth and development of behavior month by month far more clearly and graphically than could ever be possible by description.

Volume II, *Naturalistic Series*, portrays in a similar way the behavior of normal infants under the ordinary natural conditions of home life. The behavior patterns of feeding, the bath, play, and certain social relationships are portrayed as they develop month by month.

The mechanical make-up of the book is excellent. The photographs, which are enlargements from 16 mm. and 35 mm. cinema records, are clear and excellently reproduced. Each photograph has a brief explanatory note. Only one side of the page is used, and, as the pages are bound in loose leaf, they may be separated and regrouped according to the needs and desires of the individual student. The reviewer is overwhelmed with the obvious painstaking, time-consuming detail with which the pictures have been studied, selected, and finally brought together in this Atlas. It can be stated without exaggeration that the Atlas is monumental in character and the possibilities of its use in teaching and research are tremendous. Everyone interested in the field of infancy can take a just pride that such a work has come from an American clinic.

Infant Behavior was published at the same time as the Atlas and has a definite relationship to it. It summarizes the behavior characteristics in some twenty-five situations in infants from the fourth to the fifty-sixth week. After two chapters devoted to the objects and methods of study, a detailed description of the behavior pattern in the various situations follows which makes up the larger part of the book. Concluding chapters are "The Ontogenetic Patterning of Behavior," "Mental Growth and Maturation," and "The Developmental Diagnosis of Infant Behavior."

No attempt has been made in either the Atlas or accompanying volume to develop a scale of norms. What the authors have been presenting is factual data. A study of the pictures of the Atlas gives a much clearer picture of the development of infant behavior than has ever been given before. The work is of importance to pediatricians as well as to those whose field is limited to the study of infant and child development.

B. S. V.

The Crippled and Disabled. HENRY H. KESSLER, Columbia University Press, New York, 1935, p. 337.

The author defines the problem of the disabled as that of vocational maladjustment. He divides the disabled into five groups: the cripple child, the industrially disabled, the war disabled, the chronically disabled through disease, and the group disabled through blindness and loss of hearing. The problems and remedial measures in general are discussed for each group, and the various state and federal measures in force or enacted by the legislatures are given in detail. It is a most timely volume in view of the tremendous interest in social insurance, pensions, and similar matters now occupying public attention. The author has collected a mass of information which is ably analyzed and presented in a clear, direct manner.

Comments

THE legislation involving "social security" which has been proposed at Washington and concerning which hearings are now being held before congressional committees is of fundamental importance to the medical profession. The *Journal of the American Medical Association* has recently outlined the proposed legislation, and a special meeting of the House of Delegates has been called to discuss the matter. The measures proposed, if passed, will inevitably be the beginning of marked changes in the character of medical practice in the United States.

Certain measures have been proposed relating directly to the field of child welfare. Some of these measures will undoubtedly be opposed by the American Medical Association. The Academy of Pediatrics has taken no official stand in these matters although some pediatricians as individuals are supporting the child welfare measures. In brief, the child welfare measures propose an expanded program for mothers' pensions, federal cooperation in providing protection and care for homeless, dependent, and neglected children, federal aid in expanding maternal and child health programs, and care of the crippled child. The last two items in particular call for matching state funds and provide that state programs shall be approved by the Children's Bureau. This involves the old questions which were raised in opposition to the Sheppard-Towner Act.

CONSIDERABLE confusion exists in regard to the Child Labor Amendment, which is being so bitterly fought in many of the state legislatures. Unfortunately many people who do not understand the situation look upon those opposed to the amendment as being in favor of child labor. This is quite contrary to the truth. There are many individuals opposed to the amendment who are bitterly opposed to child labor. The opposition lies in the vagueness and in the unlimited power which the amendment gives to a bureaucracy at Washington. While the extreme powers which the amendment permits as depicted by some of the opponents are absurd, there is a possibility of an abuse of power which is real and not a "straw man." The writer of this is personally opposed to child labor and also to the child labor amendment—a stand that has been difficult to make clear to members of some of the women's clubs who have passed resolutions in favor of the amendment on the commendable grounds of its doing away with child labor. As a matter of fact, since the necessity for the amendment is the thing we cannot see, why establish a situation which may lead to trouble? The value of the amendment is all the more questionable in our mind in view of the recent statement of President Roosevelt that one of the real accomplishments of the New Deal was the doing away with child labor.

What irritates most is the necessity of explaining in detail that we are against child labor when we say we are not in favor of the child labor amendment. It's not the goal but the means to the end that is questioned. The proponents of the amendment unfairly classify opposition to the amendment as favoring child labor.

The Journal of Pediatrics

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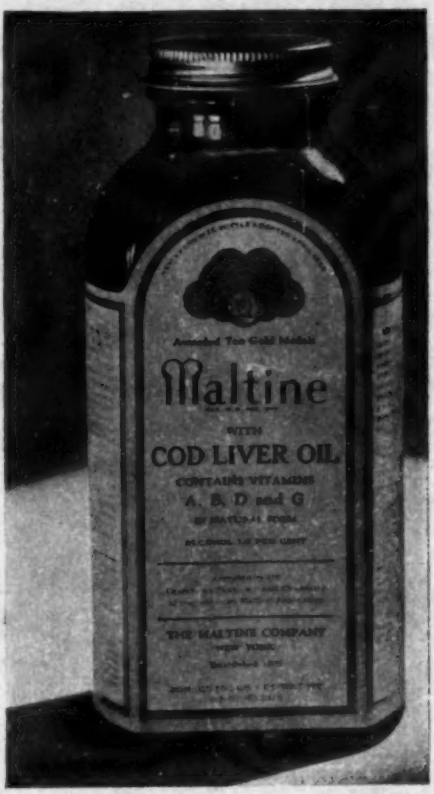

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